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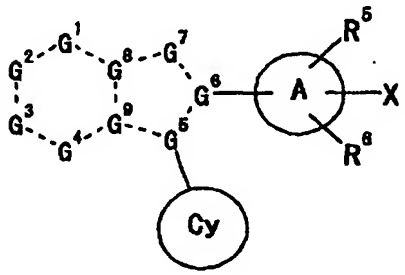
(54) FUSED-RING COMPOUNDS AND USE THEREOF AS DRUGS

(57) The present invention provides a fused ring compound of the following formula [I]



[I]

wherein each symbol is as defined in the specification, a pharmaceutically acceptable salt thereof, and a therapeutic agent for hepatitis C, which contains this compound. The compound of the present invention shows an anti-hapatitis C virus (HCV) action based on the HCV polymerase inhibitory activity, and is useful as a therapeutic agent or prophylactic agent for hepatitis C.

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Description

Technical Field

[0001] The present invention relates to a novel fused ring compound and a pharmaceutically acceptable salt thereof useful as a therapeutic agent for hepatitis C. The present invention also relates to a novel use of a certain fused ring compound or a pharmaceutically acceptable salt thereof as a therapeutic agent for hepatitis C. More particularly, the present invention relates to a therapeutic agent for hepatitis C, which contains a novel fused ring compound or a pharmaceutically acceptable salt thereof, which is effective for the prophylaxis or treatment of hepatitis C and which shows anti-hepatitis C virus (HCV) activity, particularly anti-HCV activity based on an RNA-dependent RNA polymerase inhibitory activity.

Background Art

[0002] In 1989, a main causative virus of non-A non-B posttransfusion hepatitis was found and named hepatitis C virus (HCV). Since then, several types of hepatitis viruses have been found besides type A, type B and type C, wherein hepatitis caused by HCV is called hepatitis C.

[0003] The patients infected with HCV are considered to involve several percent of the world population, and the infection with HCV characteristically becomes chronic.

[0004] HCV is an envelope RNA virus, wherein the genome is a single strand plus-strand RNA, and belongs to the genus Hepacivirus of Flavivirus (from The International Committee on Taxonomy of Viruses, International Union of Microbiological Societies). Of the same hepatitis viruses, for example, hepatitis B virus (HBV), which is a DNA virus, is eliminated by the immune system and the infection with this virus ends in an acute infection except for neonates and infants having yet immature immunological competence. In contrast, HCV somehow avoids the immune system of the host due to an unknown mechanism. Once infected with this virus, even an adult having a mature immune system frequently develops persistent infection.

[0005] When chronic hepatitis is associated with the persistent infection with HCV, it advances to cirrhosis or hepatic cancer in a high rate. Enucleation of tumor by operation does not help much, because the patient often develops recurrent hepatic cancer due to the sequela inflammation in non-cancerous parts.

[0006] Thus, an effective therapeutic method of hepatitis C is desired. Apart from the symptomatic therapy to suppress inflammation with an anti-inflammatory agent, the development of a therapeutic agent that reduces HCV to a low level free from inflammation and that eradicates HCV has been strongly demanded.

[0007] At present, a treatment with interferon is the only effective method known for the eradication of HCV. However, interferon can eradicate the virus only in about one-third of the patient population. For the rest of the patients, it has no effect or provides only a temporary effect. Therefore, an anti-HCV drug to be used in the place of or concurrently with interferon is awaited in great expectation.

[0008] In recent years, Ribavirin (1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide) has become commercially available as a therapeutic agent for hepatitis C, which is to be used concurrently with interferon. It enhances the efficacy of interferon but only to a low efficacy rate, and a different novel therapeutic agent for hepatitis C is desired.

[0009] Also, an attempt has been made to potentiate the immunocompetence of the patient with an interferon agonist, an interleukin-12 agonist and the like, thereby to eradicate the virus, but an effective pharmaceutical agent has not been found yet.

[0010] In addition, the inhibition of HCV growth, wherein HCV-specific protein is targeted, has been drawing attention these days.

[0011] The gene of HCV encodes a protein such as serine protease, RNA helicase, RNA-dependent RNA polymerase and the like. These proteins function as a specific protein essential for the growth of HCV.

[0012] One of the specific proteins, RNA-dependent RNA polymerase (hereinafter to be also briefly referred to as an HCV polymerase), is an enzyme essential for the growth of the virus. The gene replication of HCV having a plus-strand RNA gene is considered to involve synthesis of a complementary minus-strand RNA by the use of the plus-strand RNA as a template, and, using the obtained minus-strand RNA as a template, amplifying the plus-strand RNA. The portion called NS5B of a protein precursor, that HCV codes for, has been found to show an RNA-dependent RNA polymerase activity (EMBO J., 15, 12-22, 1996), and is considered to play a central role in the HCV gene replication.

[0013] Therefore, an HCV polymerase inhibitor can be a target in the development of an anti-HCV drug, and the development thereof is eagerly awaited. However, an effective HCV polymerase inhibitor has not been developed yet, like in other attempts to develop an anti-HCV drug based on other action mechanisms. As the situation stands, no pharmaceutical agent can treat hepatitis C satisfactorily.

[0014] The following discloses known compounds relatively similar to the compound of the present invention.

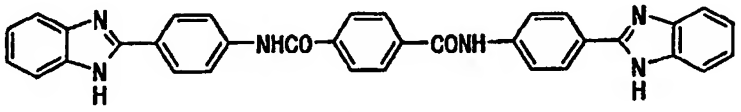
[0015] A known therapeutic agent for hepatitis C having a benzimidazole skeleton is disclosed in WO97/36866,

Japanese Patent Application under PCT laid-open under kohyo No. 2000-511899 (EP906097) and WO99/51619.

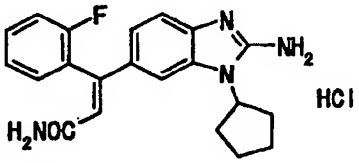
[0016] WO97/36866 discloses the following compound D and the like, and HCV helicase inhibitory activity of the compounds.

[0017] Japanese Patent Application under PCT laid-open under kohyo No. 2000-511899 (EP906097) discloses the following compound E and the like, and WO99/51619 discloses the following compound F and the like, in both of which a possibility of these compounds being effective as an HCV inhibitor is mentioned.

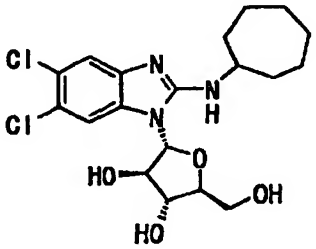
[0018] However, these publications do not include the compound disclosed in the present specification, or a disclosure suggestive thereof.



compound D



compound E

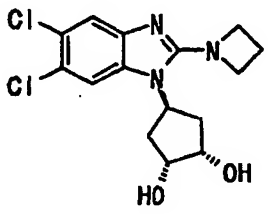


compound F

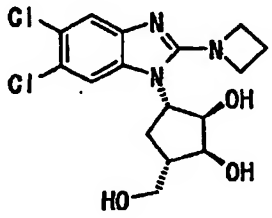
[0019] A known anti-hepatitis virus agent having a benzimidazole skeleton is disclosed in Japanese Patent Application under PCT laid-open under kohyo No. 2000-503017 (WO97/25316) and Japanese Patent Application under PCT laid-open under kohyo No. 10-505092 (WO96/7646).

[0020] WO97/25316 discloses the following compound A and the like, wherein the use thereof is for a treatment of viral infection. The target virus is a DNA virus such as hepatitis B virus and the like. However, this publication does not include the compound disclosed in the present specification or a description regarding or suggestive of HCV.

[0021] Japanese Patent Application under PCT laid-open under kohyo No. 10-505092 discloses the following compound B and the like, wherein the use thereof is for a treatment of viral infection. The target virus is a DNA virus such as herpesvirus and hepatitis B virus. However, this publication does not include the compound disclosed in the present specification or a description regarding or suggestive of HCV.



compound A



compound B

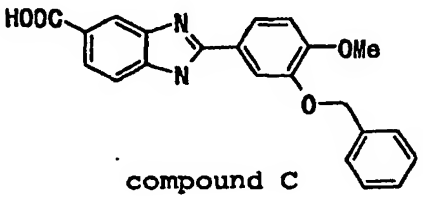
[0022] The benzimidazole derivatives having an antiviral activity have been disclosed in JP-A-3-31264, US3644382 and US3778504. In addition, WO98/37072 discloses, as a production inhibitor of tumor necrosis factor (TNF) and cyclic AMP, a benzimidazole derivative for the use as an anti-human immunodeficiency virus (HIV) agent and an anti-inflammation agent. WO98/05327 discloses, as a reverse transcriptase inhibitor, a benzimidazole derivative for the use as an anti-HIV agent. J. Med. Chem. (13(4), 697-704, 1970) discloses, as a neuraminidase inhibitor, a benzimidazole derivative for the use as an anti-influenza virus agent.

[0023] However, none of these publications includes the compound of the present invention or a description regarding

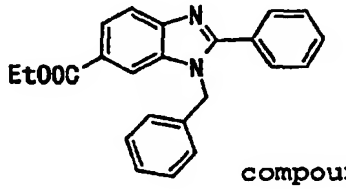
or suggestive of an anti-HCV effect.

[0024] Known benzimidazole derivatives having a pharmaceutical use other than as an antiviral agent are disclosed in JP-A-8-501318 (US5824651) and JP-A-8-134073 (US5563243). These publications disclose the following compound C and the like as a catechol diether compound, and the use thereof as an anti-inflammation agent. However, neither of the publications includes the compound of the present invention, and as the action mechanism, the former discloses phosphodiesterase IV and the latter discloses TNF. These publications do not include a description regarding or suggestive of an anti-HCV effect.

[0025] Japanese Patent Application under PCT laid-open under kohyo No. 2000-159749 (EP882718) discloses the following compound G and the like, and the use thereof for the treatment of bronchitis, glomerulonephritis and the like. However, this publication does not include the compound of the present invention, but discloses only a phosphodiesterase IV inhibitory and hypoglycemic action. This publication does not include a description regarding or suggestive of an anti-HCV effect.



compound C



compound G

[0026] WO98/50029, WO98/50030 and WO98/50031 disclose benzimidazole derivatives as an antitumor agent having a protein isoprenyl transferase action. While this publication discloses a wide scope of the claims, at least it does not include a compound analogous to the compound of the present invention or a description regarding or suggestive of an anti-HCV effect.

[0027] JP-A-8-109169 (EP694535) discloses the application of a tachykinin receptor antagonist to treat an inflammatory disease, and WO96/35713 discloses the application thereof as a growth hormone release promoter to treat a growth hormone-related disease such as osteoporosis and the like. However, none of these publications includes a description regarding or suggestive of an anti-HCV effect.

[0028] JP-A-53-14735 discloses a benzimidazole derivative as a brightener besides its pharmaceutical use, but this publication does not include the compound of the present invention.

Disclosure of the Invention

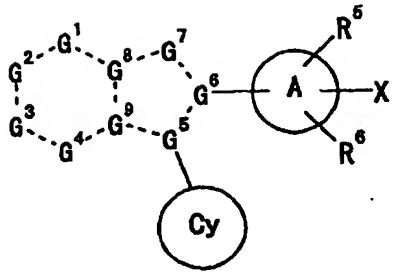
[0029] Based on the findings from the preceding studies, it has been elucidated that a pharmaceutical agent having an anti-HCV activity is effective for the prophylaxis and treatment of hepatitis C, and particularly an anti-HCV agent having an inhibitory activity on RNA-dependent RNA polymerase of HCV can be a prophylactic and therapeutic agent effective against hepatitis C and a prophylactic and therapeutic agent for the disease caused by hepatitis C.

[0030] Accordingly, the present invention provides a pharmaceutical agent having an anti-HCV activity, particularly a pharmaceutical agent having an RNA-dependent RNA polymerase inhibitory activity.

[0031] The present inventors have made an in-depth study of compounds having an anti-HCV activity, particularly RNA-dependent RNA polymerase inhibitory activity, and completed the present invention.

[0032] Thus, the present invention provides the following (1) to (43).

(1) A therapeutic agent for hepatitis C, which comprises a fused ring compound of the following formula [I] or a pharmaceutically acceptable salt thereof as an active ingredient:



[I]

wherein
a broken line is a single bond or a double bond,

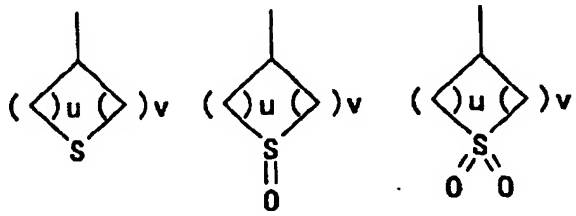
G^1	Is $C(-R^1)$ or a nitrogen atom,
G^2	is $C(-R^2)$ or a nitrogen atom,
G^3	is $C(-R^3)$ or a nitrogen atom,
G^4	is $C(-R^4)$ or a nitrogen atom,
G^5, G^6, G^8 and G^9	are each independently a carbon atom or a nitrogen atom,
G^7	is $C(-R^7)$, an oxygen atom, a sulfur atom, or a nitrogen atom optionally substituted by R^8,

wherein R^1, R^2, R^3 and R^4 are each independently,

(1) hydrogen atom,
(2) C_{1-6} alkanoyl,
(3) carboxyl,
(4) cyano,
(5) nitro,
(6) C_{1-6} alkyl optionally substituted by 1 to 3 substituent(s) selected from the following group A,
group A; halogen atom, hydroxyl group, carboxyl, amino, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl and C_{1-6} alkylamino,
(7) $-COOR^{a1}$
wherein R^{a1} is optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the following group B,
group B; halogen atom, cyano, nitro, C_{1-6} alkyl,
halogenated C_{1-6} alkyl, C_{1-6} alkanoyl,
$-(CH_2)_r-COOR^{b1}$, $-(CH_2)_r-CONR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}-COR^{b2}$, $-(CH_2)_r-NHSO_2R^{b1}$, $-(CH_2)_r-OR^{b1}$, $-(CH_2)_r-SR^{b1}$, $-(CH_2)_r-SO_2R^{b1}$ and $-(CH_2)_r-SO_2NR^{b1}R^{b2}$
wherein R^{b1} and R^{b2} are each independently hydrogen atom or C_{1-6} alkyl and r is 0 or an integer of 1 to 6,
(8) $-CONR^{a2}R^{a3}$
wherein R^{a2} and R^{a3} are each independently hydrogen atom, C_{1-6} alkoxy or optionally substituted C_{1-6} alkyl (as defined above),
(9) $-C(=NR^{a4})NH_2$
wherein R^{a4} is hydrogen atom or hydroxyl group,
(10) $-NHR^{a5}$
wherein R^{a5} is hydrogen atom, C_{1-6} alkanoyl or C_{1-6} alkylsulfonyl,
(11) $-OR^{a6}$
wherein R^{a6} is hydrogen atom or optionally substituted C_{1-6} alkyl(as defined above),
(12) $-SO_2R^{a7}$
wherein R^{a7} is hydroxyl group, amino, C_{1-6} alkyl or C_{1-6} alkylamino
or
(13) $-P(=O)(OR^{a31})_2$
wherein R^{a31} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, and

R^7 and R^8 are each hydrogen atom or optionally substituted C_{1-6} alkyl(as defined above),
ring Cy is

(1) C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the following group C, group C; hydroxyl group, halogen atom, C_{1-6} alkyl and C_{1-6} alkoxy,
(2) C_{3-8} cycloalkenyl optionally substituted by 1 to 5 substituent(s) selected from the above group C, or
(3)



wherein u and v are each independently an integer of 1 to 3,

ring A is

(1) C_{6-14} aryl,
(2) C_{3-8} cycloalkyl,
(3) C_{3-8} cycloalkenyl or
(4) heterocyclic group having 1 to 4 heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom,

R^5 and R^6 are each independently

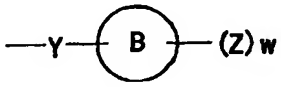
(1) hydrogen atom,
(2) halogen atom,
(3) optionally substituted C_{1-6} alkyl (as defined above) or
(4) $-OR^{a8}$
wherein R^{a8} is hydrogen atom, C_{1-6} alkyl or C_{6-14} aryl C_{1-6} alkyl, and

X is

(1) hydrogen atom,
(2) halogen atom,
(3) cyano,
(4) nitro,
(5) amino, C_{1-6} alkanoylamino,
(6) C_{1-6} alkylsulfonyl,
(7) optionally substituted C_{1-6} alkyl(as defined above),
(8) C_{2-6} alkenyl optionally substituted by 1 to 3 substituent(s) selected from the above group A,
(9) $-COOR^{a9}$
wherein R^{a9} is hydrogen atom or C_{1-6} alkyl,
(10) $-CONH-(CH_2)_1-R^{a10}$
wherein R^{a10} is optionally substituted C_{1-6} alkyl (as defined above), C_{1-6} alkoxycarbonyl or C_{1-6} alkanoylamino and 1 is 0 or an integer of 1 to 6,
(11) $-OR^{a11}$
wherein R^{a11} is hydrogen atom or optionally substituted C_{1-6} alkyl (as defined above)

or

(12)



wherein
ring B is

(1') C_{6-14} aryl,
(2') C_{3-8} cycloalkyl or
(3') heterocyclic group (as defined above),

each Z is independently

(1') a group selected from the following group D,
(2') C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the following group D,
(3') C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the following group D,
(4') C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the following group D or
(5') heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the following group D

wherein the heterocyclic group has 1 to 4 hetero-atom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom,
group D:

(a) hydrogen atom,
(b) halogen atom,
(c) cyano,
(d) nitro,
(e) optionally substituted C_{1-6} alkyl (as defined above),
(f) $-(CH_2)_t-COR^{a18}$,
(hereinafter each t means independently 0 or an integer of 1 to 6),
wherein R^{a18} is

(1") optionally substituted C_{1-6} alkyl (as defined above),
(2") C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or
(3") heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B
wherein the heterocyclic group has 1 to 4 heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom,

(g) $-(CH_2)_t-COOR^{a19}$
wherein R^{a19} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(h) $-(CH_2)_t-CONR^{a27}R^{a28}$
wherein R^{a27} and R^{a28} are each independently,

(1") hydrogen atom,
(2") optionally substituted C_{1-6} alkyl (as defined above),
(3") C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(4") C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(5") heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(6") heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
wherein the heterocycle C_{1-6} alkyl is C_{1-6} alkyl substituted by heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B, as defined above,
(7") C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, or
(8") C_{3-8} cycloalkyl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,

(i)-$(CH_2)_t-C(=NR^{a33})NH_2$
wherein R^{a33} is hydrogen atom or C_{1-6} alkyl,
(j) $-(CH_2)_t-OR^{a20}$
wherein R^{a20} is

(1") hydrogen atom,

(2") optionally substituted C_{1-6} alkyl (as defined above),
(3") optionally substituted C_{2-6} alkenyl (as defined above),
(4") C_{2-6} alkynyl optionally substituted by 1 to 3 substituent(s) selected from the above group A,
(5") C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(6") C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(7") heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(8") heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(9") C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, or
(10") C_{3-8} cycloalkyl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,

(k) $-(CH_2)_t-O-(CH_2)_p-COR^{a21}$
wherein R^{a21} is C_{1-6} alkylamino or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B, and p is 0 or an integer of 1 to 6,
(l) $-(CH_2)_t-NR^{a22}R^{a23}$
wherein R^{a22} and R^{a23} are each independently

(1") hydrogen atom,
(2") optionally substituted C_{1-6} alkyl (as defined above),
(3") C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(4") C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B or
(5") heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,

(m) $-(CH_2)_t-NR^{a29}CO-R^{a24}$
wherein R^{a29} is hydrogen atom, C_{1-6} alkyl or C_{1-6} alkanoyl, R^{a24} is optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(n) $-(CH_2)_t-NHSO_2-R^{a25}$
wherein R^{a25} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(o) $-(CH_2)_t-S(O)_q-R^{a25}$
wherein R^{a25} is as defined above, and q is 0, 1 or 2,
and
(p)$-(CH_2)_t-SO_2-NHR^{a26}$
wherein R^{a26} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or heterocyclic group optionally substituted by to 5 substituent(s) selected from the above group B,

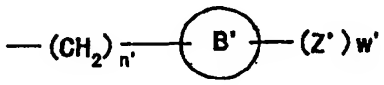
w is an integer of 1 to 3, and
Y is

(1') a single bond,
(2') C_{1-6} alkylene,
(3') C_{2-6} alkenylene,
(4') $-(CH_2)_m-O-(CH_2)_n-$,
(hereinafter m and n are each independently 0 or an integer of 1 to 6),
(5') -CO-,
(6') $-CO_2-(CH_2)_n-$,
(7') $-CONH-(CH_2)_n-NH-$,
(8') $-NHCO_2-$,
(9') -NHCONH-,
(10') $-O-(CH_2)_n-CO-$,
(11') $-O-(CH_2)_n-O-$,
(12') $-SO_2-$,
(13') $-(CH_2)_m-NR^{a12}-(CH_2)_n-$
wherein R^{a12} is

(1") hydrogen atom,
(2") optionally substituted C_{1-6} alkyl (as defined above),
(3") C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(4") C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(5") $-COR^{b5}$
wherein R^{b5} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(6") $-COOR^{b5}$ (R^{b5} is as defined above) or
(7") $-SO_2R^{b5}$ (R^{b5} is as defined above),

(14') $-NR^{a12}CO-$ (R^{a12} is as defined above),
(15') $-CONR^{a13}-(CH_2)_n-$
wherein R^{a13} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(16') $-CONH-CHR^{a14}-$
wherein R^{a14} is C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(17') $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$
wherein R^{a15} and R^{a16} are each independently

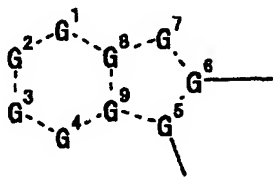
(1") hydrogen atom,
(2") carboxyl,
(3") C_{1-6} alkyl,
(4") $-OR^{b6}$
wherein R^{b6} is C_{1-6} alkyl or C_{6-14} aryl C_{1-6} alkyl, or
(5") $-NHR^{b7}$
wherein R^{b7} is hydrogen atom, C_{1-6} alkyl, C_{1-6} alkanoyl or C_{6-14} aryl C_{1-6} alkyloxycarbonyl, or R^{a15} is optionally
(6")



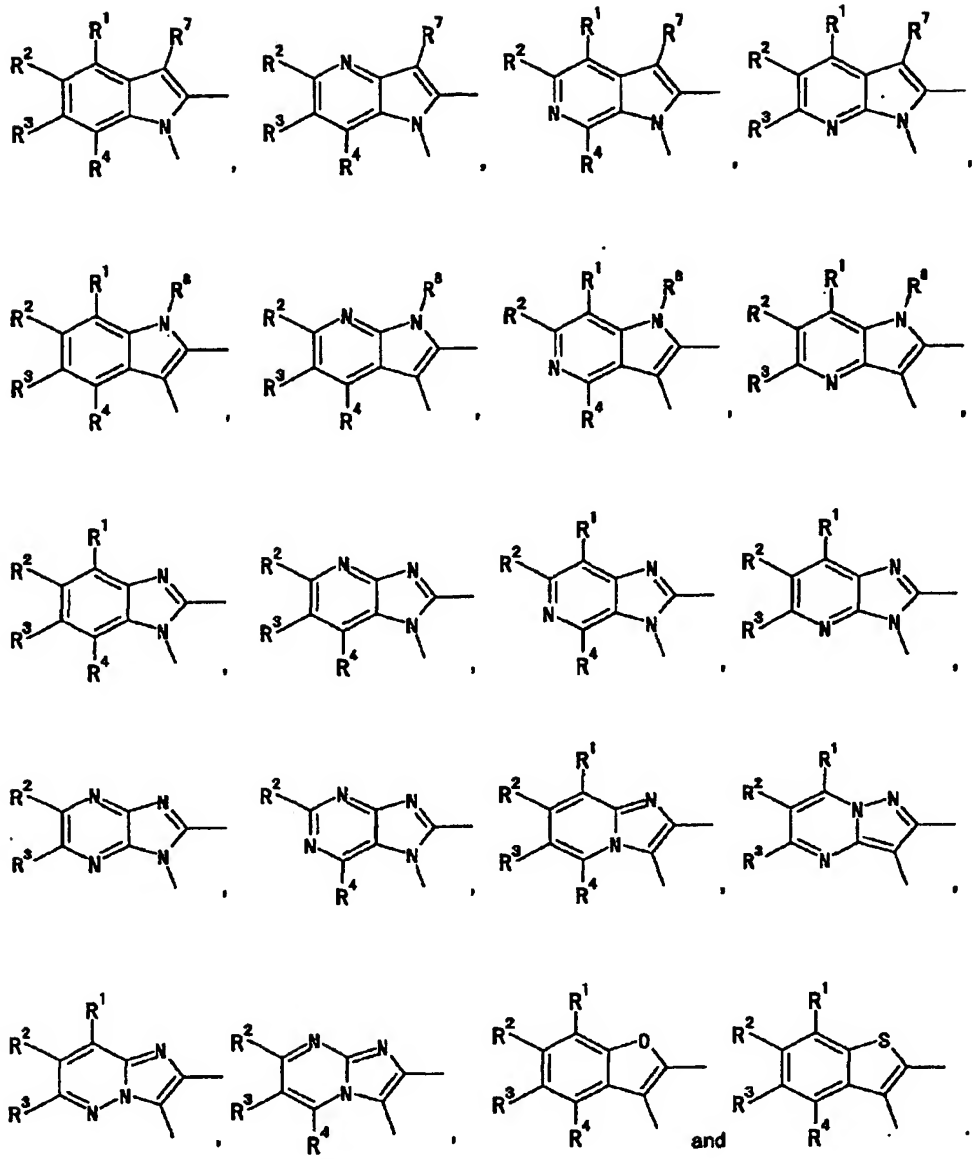
wherein n', ring B', Z' and w' are the same as the above-mentioned n, ring B, Z and w, respectively, and may be the same as or different from the respective counterparts,

(18')-$(CH_2)_n-NR^{a12}-CHR^{a15}-$ (R^{a12} and R^{a15} are each as defined above),
(19') $-NR^{a17}SO_2-$
wherein R^{a17} is hydrogen atom or C_{1-6} alkyl or
(20') $-S(O)_e-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$ (e is 0, 1 or 2, R^{a15} and R^{a16} are each as defined above).

(2) The therapeutic agent of (1) above, wherein 1 to 4 of the G^1, G^2, G^3, G^4, G^5, G^6, G^7, G^8 and G^9 is (are) a nitrogen atom.
(3) The therapeutic agent of (2) above, wherein G^2 is $C(-R^2)$ and G^6 is a carbon atom.
(4) The therapeutic agent of (2) or (3) above, wherein G^5 is a nitrogen atom.
(5) The therapeutic agent of (1) above, wherein, in formula [I], the moiety

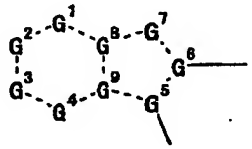


is a fused ring selected from

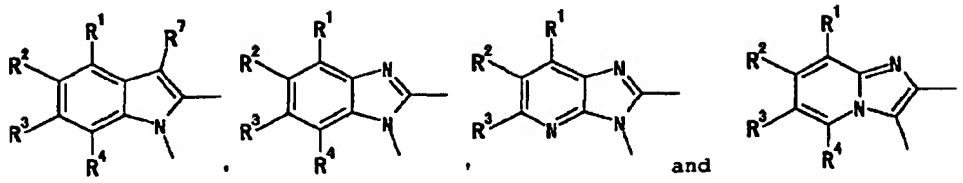


and

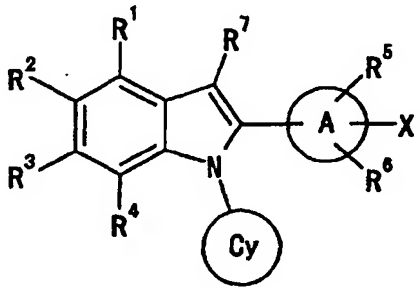
(6) The therapeutic agent of (5) above, wherein, in formula [I], the moiety



is a fused ring selected from



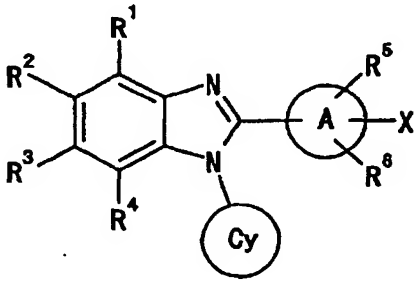
(7) The therapeutic agent of (6) above, which comprises a fused ring compound of the following formula [I-1]



[I-1]

wherein each symbol is as defined in (1),
or a pharmaceutically acceptable salt thereof as an active ingredient.

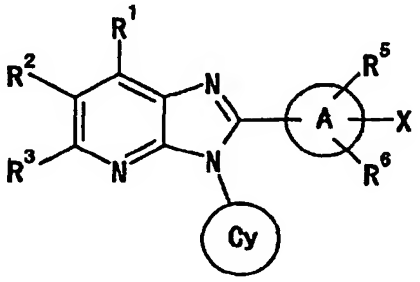
(8) The therapeutic agent of (6) above, which comprises a fused ring compound of the following formula [I-2]



[I-2]

wherein each symbol is as defined in (1),
or a pharmaceutically acceptable salt thereof as an active ingredient.

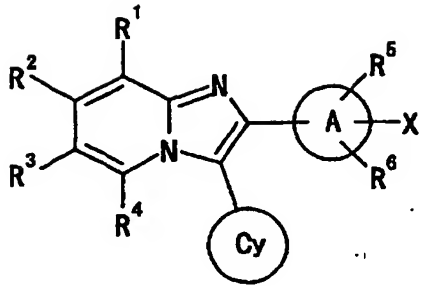
(9) The therapeutic agent of (6) above, which comprises a fused ring compound of the following formula [I-3]



[I-3]

wherein each symbol is as defined in (1),
or a pharmaceutically acceptable salt thereof as an active ingredient.

(10) The therapeutic agent of (6) above, which comprises a fused ring compound of the following formula [I-4]



[I-4]

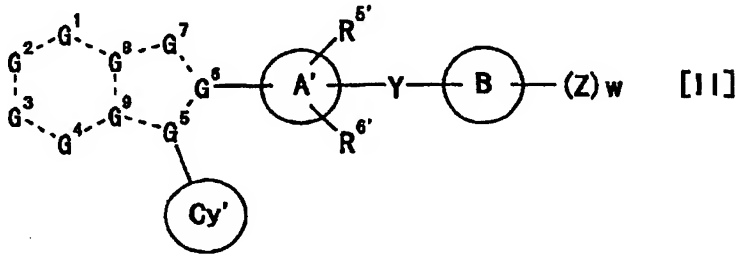
wherein each symbol is as defined in (1),
or a pharmaceutically acceptable salt thereof as an active ingredient.

(11) The therapeutic agent of any of (1) to (10) above, wherein at least one of R^1, R^2, R^3 and R^4 is carboxyl, $-COOR^{a1}$, $-CONR^{a2}R^{a3}$ or $-SO_2R^{a7}$ wherein R^{a1}, R^{a2}, R^{a3} and R^{a7} are as defined in (1).

(12) The therapeutic agent of any of (1) to (11) above, wherein the ring Cy is cyclopentyl, cyclohexyl, cycloheptyl or tetrahydrothiopyranyl.

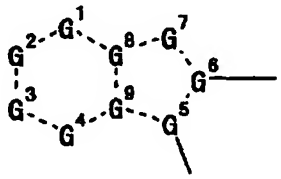
(13) The therapeutic agent of any of (1) to (12) above, wherein the ring A is C_{6-14} aryl.

(14) A fused ring compound of the following formula [II]

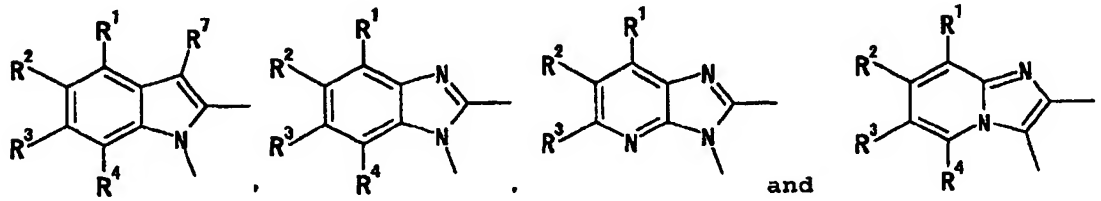


[II]

wherein
the moiety



is a fused ring selected from



and

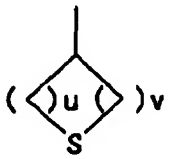
wherein R^1, R^2, R^3 and R^4 are each independently,

(1) hydrogen atom,

(2) C_{1-6} alkanoyl,
(3) carboxyl,
(4) cyano,
(5) nitro,
(6) C_{1-6} alkyl optionally substituted by 1 to 3 substituent(s) selected from the following group A,
group A; halogen atom, hydroxyl group, carboxyl, amino, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl and C_{1-6} alkylamino,
(7) $-COOR^{a1}$
wherein R^{a1} is optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the following group B,
group B; halogen atom, cyano, nitro, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkanoyl, $-(CH_2)_r-COOR^{b1}$, $-(CH_2)_r-CONR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}-COR^{b2}$, $-(CH_2)_r-NHSO_2R^{b1}$, $-(CH_2)_r-OR^{b1}$, $-(CH_2)_r-SR^{b1}$, $-(CH_2)_r-SO_2R^{b1}$ and $-(CH_2)_r-SO_2NR^{b1}R^{b2}$
wherein R^{b1} and R^{b2} are each independently hydrogen atom or C_{1-6} alkyl and r is 0 or an integer of 1 to 6,
(8) $-CONR^{a2}R^{a3}$
wherein R^{a2} and R^{a3} are each independently hydrogen atom, C_{1-6} alkoxy or optionally substituted C_{1-6} alkyl (as defined above),
(9) $-C(=NR^{a4})NH_2$
wherein R^{a4} is hydrogen atom or hydroxyl group,
(10) $-NHR^{a5}$
wherein R^{a5} is hydrogen atom, C_{1-6} alkanoyl or C_{1-6} alkylsulfonyl,
(11) $-OR^{a6}$
wherein R^{a6} is hydrogen atom or optionally substituted C_{1-6} alkyl (as defined above),
(12) $-SO_2R^{a7}$
wherein R^{a7} is hydroxyl group, amino, C_{1-6} alkyl or C_{1-6} alkylamino
or
(13) $-P(=O)(OR^{a31})_2$
wherein R^{a31} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, and
R^7 is hydrogen atom or optionally substituted
C_{1-6} alkyl (as defined above),

ring Cy' is

(1) C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the following group C, group C; hydroxyl group, halogen atom, C_{1-6} alkyl and C_{1-6} alkoxy, or
(2)



wherein u and v are each independently an integer of 1 to 3,

ring A' is a group selected from a group consisting of phenyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, cyclohexyl, cyclohexenyl, furyl and thienyl,
$R^{5'}$ and $R^{6'}$ are each independently

(1) hydrogen atom,
(2) halogen atom,
(3) optionally substituted C_{1-6} alkyl (as defined above) or
(4) hydroxyl group

ring B is

(1) C_{6-14} aryl,

(2) C_{3-8} cycloalkyl or
(3) heterocyclic group having 1 to 4 heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom,

each Z is independently

(1) a group selected from the following group D,
(2) C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the following group D,
(3) C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the following group D,
(4) C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the following group D or
(5) heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the following group D
wherein the heterocyclic group has 1 to 4 heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom, group D:

(a) hydrogen atom,
(b) halogen atom,
(c) cyano,
(d) nitro,
(e) optionally substituted C_{1-6} alkyl (as defined above),
(f) $-(CH_2)_t-COR^{a18}$,
(hereinafter each t means independently 0 or an integer of 1 to 6),
wherein R^{a18} is

(1') optionally substituted C_{1-6} alkyl (as defined above),
(2') C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or
(3') heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B
wherein the heterocyclic group has 1 to 4 heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom,

(g) $-(CH_2)_t-COOR^{a19}$
wherein R^{a19} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(h) $-(CH_2)_t-CONR^{a27}R^{a28}$
wherein R^{a27} and R^{a28} are each independently,

(1") hydrogen atom,
(2") optionally substituted C_{1-6} alkyl (as defined above),
(3") C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(4") C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(5") heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(6") heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
wherein the heterocycle C_{1-6} alkyl is C_{1-6} alkyl substituted by heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B, as defined above,
(7") C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, or
(8") C_{3-8} cycloalkyl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,

(i) $-(CH_2)_t-C(=NR^{a33})NH_2$
wherein R^{a33} is hydrogen atom or C_{1-6} alkyl,
(j) $-(CH_2)_t-OR^{a20}$
wherein R^{a20} is

(1') hydrogen atom,

(2') optionally substituted C_{1-6} alkyl (as defined above),
(3') optionally substituted C_{2-6} alkenyl (as defined above),
(4') C_{2-6} alkynyl optionally substituted by 1 to 3 substituent(s) selected from the above group A,
(5') C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(6') C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(7') heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(8') heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(9') C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, or
(10') C_{3-8} cycloalkyl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,

(k) - $(CH_2)_t$-O-$(CH_2)_p$-COR^{a21}
wherein R^{a21} is C_{1-6} alkylamino or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B, and p is 0 or an integer of 1 to 6,
(l) -$(CH_2)_t$-$NR^{a22}R^{a23}$
wherein R^{a22} and R^{a23} are each independently

(1') hydrogen atom,
(2') optionally substituted C_{1-6} alkyl (as defined above),
(3') C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(4') C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B or
(5') heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,

(m) -$(CH_2)_t$-$NR^{a29}CO$-R^{a24}
wherein R^{a29} is hydrogen atom, C_{1-6} alkyl or C_{1-6} alkanoyl, R^{a24} is optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(n)-$(CH_2)_t$-$NHSO_2$-R^{a25}
wherein R^{a25} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) , C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(o) -$(CH_2)_t$-$S(O)_q$-R^{a25}
wherein R^{a25} is as defined above, and q is 0, 1 or 2,
and
(p) -$(CH_2)_t$-SO_2-NHR^{a26}
wherein R^{a26} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from the above group B,

is an integer of 1 to 3, and
is

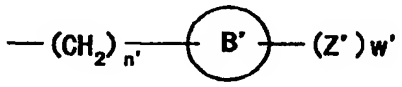
(1) a single bond,
(2) C_{1-6} alkylene,
(3) C_{2-6} alkenylene,
(4) -$(CH_2)_m$-O-$(CH_2)_n$-,
(hereinafter m and n are each independently 0 or an integer of 1 to 6),
(5) -CO-,
(6) -CO_2-$(CH_2)_n$-,
(7) -CONH-$(CH_2)_n$-NH-,
(8) -$NHCO_2$-,

(9) -NHCONH-,
(10) -O-$(CH_2)_n$-CO-,
(11) -O-$(CH_2)_n$-O-,
(12) -SO_2-,
(13) -$(CH_2)_m$-NR^{a12}-$(CH_2)_n$-
wherein R^{a12} is

(1') hydrogen atom,
(2') optionally substituted C_{1-6} alkyl (as defined above),
(3') C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(4') C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(5') -COR^{b5}
wherein R^{b5} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above), C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(6') -$COOR^{b5}$ (R^{b5} is as defined above) or
(7') -SO_2R^{b5} (R^{b5} is as defined above),

(14) -$NR^{a12}CO$- (R^{a12} is as defined above),
(15) -$CONR^{a13}$-$(CH_2)_n$-
wherein R^{a13} is hydrogen atom, optionally substituted C_{1-6} alkyl (as defined above) or C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(16) -CONH-CHR^{a14}-
wherein R^{a14} is C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from the above group B,
(17) -O-$(CH_2)_m$-$CR^{a15}R^{a16}$-$(CH_2)_n$-
wherein R^{a15} and R^{a16} are each independently

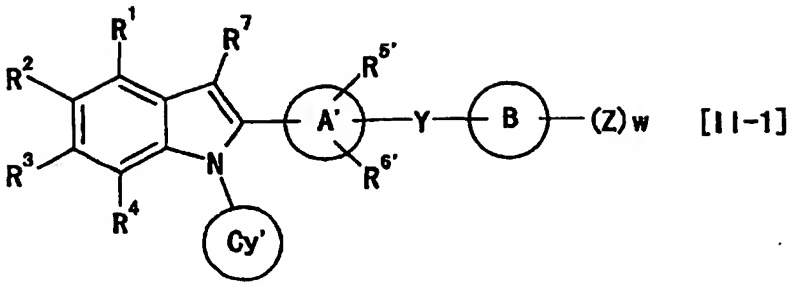
(1') hydrogen atom,
(2') carboxyl,
(3') C_{1-6} alkyl,
(4') -OR^{b6}
wherein R^{b6} is C_{1-6} alkyl or C_{6-14} aryl C_{1-6} alkyl, or
(5') -NHR^{b7}
wherein R^{b7} is hydrogen atom, C_{1-6} alkyl, C_{1-6} alkanoyl or C_{6-14} aryl C_{1-6} alkyloxycarbonyl, or R^{a15} is optionally
(6')



wherein n', ring B', Z' and w' are the same as the above-mentioned n, ring B, Z and w, respectively, and may be the same as or different from the respective counterparts,

(18) -$(CH_2)_n$-NR^{a12}-CHR^{a15}- (R^{a12} and R^{a15} are each as defined above),
(19) -$NR^{a17}SO_2$-
wherein R^{a17} is hydrogen atom or C_{1-6} alkyl or
(20) -$S(O)_e$-$(CH_2)_m$-$CR^{a15}R^{a16}$-$(CR_2)_n$- (e is 0, 1 or 2, R^{a15} and R^{a16} are each as defined above),

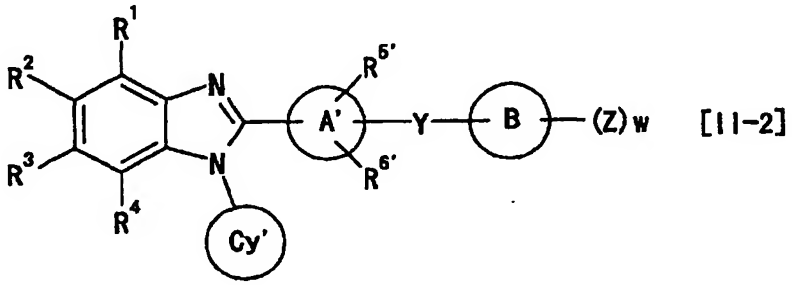
or a pharmaceutically acceptable salt thereof.
(15) The fused ring compound of (14) above, which is represented by the following formula [II-1]



[II-1]

wherein each symbol is as defined in (14),
or a pharmaceutically acceptable salt thereof.

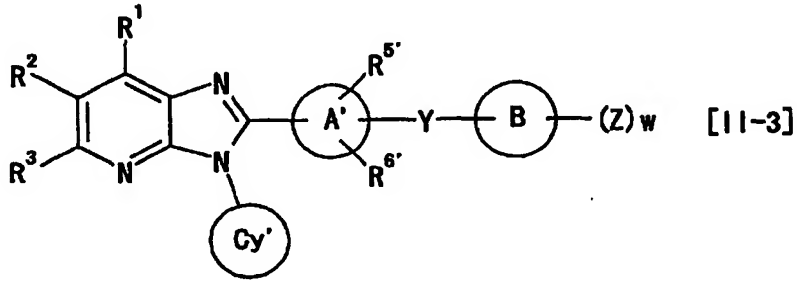
(16) The fused ring compound of (14) above, which is represented by the following formula [II-2]



[II-2]

wherein each symbol is as defined in (14),
or a pharmaceutically acceptable salt thereof.

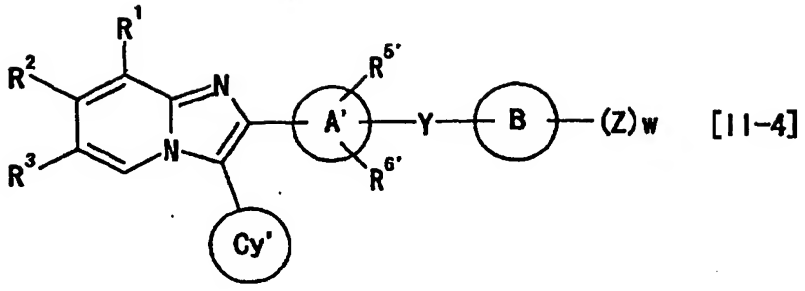
(17) The fused ring compound of (14) above, which is represented by the following formula [II-3]



[II-3]

wherein each symbol is as defined in (14),
or a pharmaceutically acceptable salt thereof.

(18) The fused ring compound of (14) above, which is represented by the following formula [II-4]



[II-4]

wherein each symbol is as defined in (14),
or a pharmaceutically acceptable salt thereof.

(19) The fused ring compound of any of (14) to (18) above, wherein at least one of R^1, R^2, R^3 and R^4 is carboxyl, $-COOR^{a1}$ or $-SO_2R^{a7}$ wherein R^{a1} and R^{a7} are as defined in (14), or a pharmaceutically acceptable salt thereof.

(20) The fused ring compound of (19) above, wherein at least one of R^1, R^2, R^3 and R^4 is carboxyl or $-COOR^{a1}$ wherein R^{a1} is as defined in (14), or a pharmaceutically acceptable salt thereof.

(21) The fused ring compound of (20) above, wherein R^2 is carboxyl and R^1, R^3 and R^4 are hydrogen atoms, or a pharmaceutically acceptable salt thereof.

(22) The fused ring compound of any of (14) to (21) above, wherein the ring Cy' is cyclopentyl, cyclohexyl, cycloheptyl or tetrahydrothiopyranyl, or a pharmaceutically acceptable salt thereof.

(23) The fused ring compound of (22) above, wherein the ring Cy' is cyclopentyl, cyclohexyl or cycloheptyl, or a pharmaceutically acceptable salt thereof.

(24) The fused ring compound of any of (14) to (23) above, wherein the ring A' is phenyl, pyridyl, pyrazinyl, pyrimidinyl or pyridazinyl, or a pharmaceutically acceptable salt thereof.

(25) The fused ring compound of (24) above, wherein the ring A' is phenyl or pyridyl, or a pharmaceutically acceptable salt thereof.

(26) The fused ring compound of (25) above, wherein the ring A' is phenyl, or a pharmaceutically acceptable salt thereof.

(27) The fused ring compound of any of (14) to (26) above, wherein the Y is $-(CH_2)_m-O-(CH_2)_n-$, $-NHCO_2-$, $-CONHCHR^{a14}-$, $-(CH_2)_m-NR^{a12}-(CH_2)_n-$, $-CONR^{a13}-(CH_2)_n-$, $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$ or $-(CH_2)_n-NR^{a12}-CHR^{a15}-$ (wherein each symbol is as defined in (14)), or a pharmaceutically acceptable salt thereof.

(28) The fused ring compound of (27) above, wherein the Y is $-(CH_2)_m-O-(CH_2)_n-$ or $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$ (wherein each symbol is as defined in (14)), or a pharmaceutically acceptable salt thereof.

(29) The fused ring compound of (28) above, wherein the Y is $-(CH_2)_m-O-(CH_2)_n-$ wherein each symbol is as defined in (14), or a pharmaceutically acceptable salt thereof.

(30) The fused ring compound of any of (14) to (29) above, wherein the R^2 is carboxyl, R^1, R^3 and R^4 are hydrogen atoms, the ring Cy' is cyclopentyl, cyclohexyl or cycloheptyl, and the ring A' is phenyl, or a pharmaceutically acceptable salt thereof.

(31) The fused ring compound of the formula [I] or a pharmaceutically acceptable salt thereof, which is selected from the group consisting of

ethyl 2-[4-(3-bromophenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylate (Example 1),
2-[4-(3-bromophenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 2),
ethyl 1-cyclohexyl-2-(4-hydroxyphenyl)benzimidazole-5-carboxylate (Example 3),
ethyl 2-[4-(2-bromo-5-chlorobenzyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylate (Example 4),
ethyl 2-{4-[2-(4-chlorophenyl)-5-chlorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 5),
2-{4-[2-(4-chlorophenyl)-5-chlorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 6),
ethyl 2-[4-(2-bromo-5-methoxybenzyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylate (Example 7),
ethyl 2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 8),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 9),
ethyl 1-cyclohexyl-2-{4-[(E)-2-phenylvinyl]phenyl}benzimidazole-5-carboxylate (Example 10),
1-cyclohexyl-2-{4-[(E)-2-phenylvinyl]phenyl}benzimidazole-5-carboxylic acid (Example 11),

2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 12),
2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole-5-carboxamide (Example 13),
2-(4-benzyloxyphenyl)-5-cyano-1-cyclopentylbenzimidazole (Example 14),
2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole-5-carboxamide oxime (Example 15),
ethyl 1-cyclohexyl-2-{4-[{4-(4-fluorophenyl)-2-methyl-5-thiazolyl}methoxy]phenyl}benzimidazole-5-carboxylate (Example 16),
1-cyclohexyl-2-{4-[{4- (4-fluorophenyl)-2-methyl-5-thiazolyl}-methoxy]phenyl}benzimidazole-5-carboxylic acid (Example 17),
ethyl 1-cyclohexyl-2-(2-fluoro-4-hydroxyphenyl)benzimidazole-5-carboxylate (Example 18),
ethyl 2-{4-[bis(3-fluorophenyl)methoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 19),
2-{4-[bis(3-fluorophenyl)methoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 20),
ethyl 1-cyclopentyl-2- (4-nitrophenyl)benzimidazole-5-carboxylate (Example 21),
ethyl 2-(4-aminophenyl)-1-cyclopentylbenzimidazole-5-carboxylate (Example 22),
ethyl 2-(4-benzoylaminophenyl)-1-cyclopentylbenzimidazole-5-carboxylate (Example 23),
2-(4-benzoylaminophenyl)-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 24),
ethyl 2-{4-[3-(3-chlorophenyl)phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 25),
2-{4-[3-(3-chlorophenyl)phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 26),
ethyl 2-[4-(3-acetoxyphenyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylate (Example 27),
ethyl 1-cyclohexyl-2-[4-(3-hydroxyphenyloxy)phenyl]benzimidazole-5-carboxylate (Example 28),
ethyl 1-cyclohexyl-2-{4-[3-(4-pyridylmethoxy)phenyloxy]phenyl}-benzimidazole-5-carboxylate (Example 29),
1-cyclohexyl-2-{4-[3-(4-pyridylmethoxy)phenyloxy]phenyl}-benzimidazole-5-carboxylic acid (Example 30),
2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole (Example 31),
ethyl 2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole-5- carboxylate (Example 32),
2-(4-benzyloxyphenyl)-1-cyclopentyl-N,N-dimethylbenzimidazole-5-carboxamide (Example 33),
2-(4-benzyloxyphenyl)-1-cyclopentyl-N-methoxy-N-methylbenzimidazole-5-carboxamide (Example 34),
2-(4-benzyloxyphenyl)-1-cyclopentyl-5-(1-hydroxy-1-methylethyl)benzimidazole (Example 35),
5-acetyl-2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole (Example 36),
2-(4-benzyloxyphenyl)-1-cyclopentyl-N-(2-dimethylaminoethyl)-benzimidazole-5-carboxamide dihydrochloride (Example 37),
2-(4-benzyloxyphenyl)-1-cyclopentyl-5-nitrobenzimidazole (Example 38),
5-amino-2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole hydrochloride (Example 39),
5-acetylamino-2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole (Example 40),
2-(4-benzyloxyphenyl)-1-cyclopentyl-5-methanesulfonyl-aminobenzimidazole (Example 41),
5-sulfamoyl-2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazole (Example 42),
2-[4-(4-tert-butylbenzyloxy)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 43),
2-[4-(4-carboxybenzyloxy)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 44),
2-[4-(4-chlorobenzyloxy)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 45),
2-{4-[(2-chloro-5-thienyl)methoxy]phenyl}-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 46),
1-cyclopentyl-2-[4- (4-trifluoromethylbenzyloxy)phenyl]-benzimidazole-5-carboxylic acid (Example 47),
1-cyclopentyl-2-[4-(4-methoxybenzyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 48),
1-cyclopentyl-2-[4-(4-pyridylmethoxy)phenyl]benzimidazole-5-carboxylic acid hydrochloride (Example 49),
1-cyclopentyl-2-[4-(4-methylbenzyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 50),
1-cyclopentyl-2-{4-[(3,5-dimethyl-4-isoxazolyl)methoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 51),
1-cyclopentyl-2-(4-hydroxyphenyl)benzimidazole-5-carboxylic acid (Example 52),
[2-(4-benzyloxyphenyl)-1-cyclopentylbenzimidazol-5-yl]-carbonylaminoacetic acid (Example 53),
2-[4-(2-chlorobenzyloxy)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 54),
2-[4-(3-chlorobenzyloxy)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 55),
2-(4-benzyloxyphenyl)-3-cyclopentylbenzimidazole-5-carboxylic acid (Example 56),
2-[4-(benzenesulfonylamino)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 57),
1-cyclopentyl-2-[4-(3,5-dichlorophenylcarbonylamino)phenyl]-benzimidazole-5-carboxylic acid (Example 58),
2-{4-[(4-chlorophenyl)carbonylamino]phenyl}-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 59),
2-{4-[(4-tert-butylphenyl)carbonylamino]phenyl}-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 60),
2-{4-[(4-benzyloxyphenyl)carbonylamino]phenyl}-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 61),
trans-4-[2-(4-benzyloxyphenyl)-5-carboxybenzimidazol-1-yl]cyclohexan-1-ol (Example 62),

trans-1-[2-(4-benzyloxyphenyl)-5-carboxybenzimidazol-1-yl]-4-methoxycyclohexane (Example 63),
2-(4-benzyloxyphenyl)-5-carboxymethyl-1-cyclopentylbenzimidazole (Example 64),
2-[1-benzyloxycarbonyl-4-piperidyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 65),
2-[(4-cyclohexylphenyl)carbonylamino]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 66),
1-cyclopentyl-2-[4- (3,5-dichlorobenzyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 67),
1-cyclopentyl-2-[4- (3,4-dichlorobenzyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 68),
1-cyclopentyl-2-[4-(phenylcarbamoylamino)phenyl]benzimidazole-5-carboxylic acid (Example 69),
1-cyclopentyl-2-[4-(diphenylmethoxy)phenyl]benzimidazole-5-carboxylic acid (Example 70),
1-cyclopentyl-2-(4-phenethyloxyphenyl)benzimidazole-5-carboxylic acid (Example 71),
trans-1-[2-(4-benzyloxyphenyl)-5-carboxybenzimidazol-1-yl]-4-tert-butylcyclohexane (Example 72),
2-(4-benzyloxyphenyl)-5-carboxymethoxy-1-cyclopentylbenzimidazole (Example 73),
2-(4-benzylaminophenyl)-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 74),
2-[4-(N-benzenesulfonyl-N-methylamino)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 75),
2-[4-(N-benzyl-N-methylamino)phenyl]-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 76),
1-cyclohexyl-2-(4-phenethylphenyl)benzimidazole-5-carboxylic acid (Example 77),
2-(1-benzyl-4-piperidyl)-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 78),
2-(1-benzoyl-4-piperidyl)-1-cyclopentylbenzimidazole-5-carboxylic acid (Example 79),
1-cyclopentyl-2-[1-(p-toluenesulfonyl)-4-piperidyl]benzimidazole-5-carboxylic acid (Example 80),
1-cyclohexyl-2-[4-(3,5-dichlorobenzyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 81),
1-cyclohexyl-2-[4- (diphenylmethoxy)phenyl]benzimidazole-5-carboxylic acid (Example 82),
1-cyclohexyl-2- [4- (3,5-di-tert-butylbenzyloxy)phenyl]-benzimidazole-5-carboxylic acid (Example 83),
2-(4-benzyloxyphenyl)-1-(4-methylcyclohexyl)benzimidazole-5-carboxylic acid (Example 84),
1-cyclohexyl-2-{4-[2-(2-naphthyl)ethoxy]phenyl}benzimidazole-5-carboxylic acid (Example 85),
1-cyclohexyl-2-[4-(1-naphthyl)methoxyphenyl]benzimidazole-5-carboxylic acid (Example 86),
1-cyclohexyl-2-[4-(dibenzylamino)phenyl]benzimidazole-5-carboxylic acid (Example 87),
2-[4-(2-biphenylylmethoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 88),
2-(4-benzyloxyphenyl)-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 89),
1-cyclohexyl-2-[4- (dibenzylmethoxy)phenyl]benzimidazole-5-carboxylic acid (Example 90),
2-(4-benzoylmethoxyphenyl)-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 91),
2-(4-benzyl-1-piperazinyl)-1-cyclohexylbenzimidazole-5-carboxylic acid dihydrochloride (Example 92),
1-cyclohexyl-2-[4-(3,3-diphenylpropyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 93),
2-[4-(3-chloro-6-phenylbenzyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 94),
2-(4-benzyloxypiperidino)-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 95),
1-cyclohexyl-2-{4-[2-(phenoxy)ethoxy]phenyl}benzimidazole-5-carboxylic acid (Example 96),
1-cyclohexyl-2-[4-(3-phenylpropyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 97),
1-cyclohexyl-2-[4-(5-phenylpentyloxy)phenyl]benzimidazole-5-carboxylic acid (Example 98),
2-(3-benzyloxy-5-isoxazolyl)-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 99),
2-(2-benzyloxy-5-pyridyl)-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 100),
1-cyclohexyl-2-{4-[2-(3,4,5-trimethoxyphenyl)ethoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 101),
2-(4-benzyloxyphenyl)-1-(4,4-dimethylcyclohexyl)benzimidazole-5-carboxylic acid (Example 102),
1-cyclohexyl-2-{4-[2-(1-naphthyl)ethoxy]phenyl}benzimidazole-5-carboxylic acid (Example 103),
2-[4-(2-benzyloxyphenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 104),
2-[4-(3-benzyloxyphenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 105),
1-cyclohexyl-2-[4-(2-hydroxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 106),
1-cyclohexyl-2-[4-(3-hydroxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 107),
1-cyclohexyl-2-[4-(2-methoxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 108),
1-cyclohexyl-2-[4-(3-methoxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 109),
1-cyclohexyl-2-[4-(2-propoxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 110),
1-cyclohexyl-2-[4-(3-propoxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 111),
1-cyclohexyl-2-{4-[2-(3-methyl-2-butenyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 112),
1-cyclohexyl-2-{4-[3-(3-methyl-2-butenyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 113),
1-cyclohexyl-2-[4-(2-isopentyloxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 114),
1-cyclohexyl-2-[4-(3-isopentyloxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 115),
1-cyclohexyl-2-{4-[2-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)ethoxy]phenyl}benzimidazole-5-carboxylic acid (Example 116),

1-cyclohexyl-2-{4-[2-(4-trifluoromethylphenyl)benzyloxy]-phenyl}benzimidazole-5-carboxylic acid (Example 117),
2-{4-[bis(4-chlorophenyl) methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 118),
1-cyclohexyl-2-{4-[2-(4-methoxyphenyl)ethoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 119),
1-cyclohexyl-2-{4-[2-(2-methoxyphenyl)ethoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 120),
1-cyclohexyl-2-{4-[2-(3-methoxyphenyl)ethoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 121),
2-(4-benzyloxyphenyl)-1-cycloheptylbenzimidazole-5-carboxylic acid (Example 122),
1-cyclohexyl-2-[4-(2-phenethyloxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 123),
1-cyclohexyl-2-[4-(3-phenethyloxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 124),
1-cyclohexyl-2-[4-(2,2-diphenylethoxy)phenyl]benzimidazole-5-carboxylic acid (Example 125),
2-(4-benzyloxyphenyl)-1-(3-cyclohexenyl)benzimidazole-5-carboxylic acid (Example 126),
cis-1-[2-(4-benzyloxyphenyl)-5-carboxybenzimidazol-1-yl]-4-fluorocyclohexane (Example 127),
1-cyclohexyl-2-[4-(2-phenoxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 128),
1-cyclohexyl-2-[4-(3-phenoxyphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 129),
2-{4-[(2R)-2-benzyloxycarbonylamino-2-phenylethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 130),
1-cyclohexyl-2-{2-fluoro-4-[2-(4-trifluoromethylphenyl)-benzyloxy]phenyl}benzimidazole-5-carboxylic acid (Example 131),
2-[4-(4-benzyloxyphenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 132),
2-{4-[bis(4-methylphenyl)methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 133),
2-{4-[bis(4-fluorophenyl)methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 134),
1-cyclohexyl-6-methoxy-2-[4-(3-phenylpropoxy)phenyl]-benzimidazole-5-carboxylic acid (Example 135),
1-cyclohexyl-6-hydroxy-2-[4-(3-phenylpropoxy)phenyl]-benzimidazole-5-carboxylic acid (Example 136),
1-cyclohexyl-6-methyl-2- [4- (3-phenylpropoxy) phenyl]benzimidazole-5-carboxylic acid (Example 137),
2-{4-[2-(2-benzyloxyphenyl)ethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 138),
2-{4-[2-(3-benzyloxyphenyl)ethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 139),
2-[4-(2-carboxymethyloxyphenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 140),
2-[4-(3-carboxymethyloxyphenoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 141),
2-{4-[3-chloro-6-(4-methylphenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 142),
2-{4-[3-chloro-6-(4-methoxyphenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 143),
1-cyclohexyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-benzyloxy]phenyl}benzimidazole-5-carboxylic acid (Example 144),
2-{4-[2-(4-tert-butylphenyl)-5-chlorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 145),
2-{4-(3-chloro-6-phenylbenzyloxy)-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 146),
2-{4-[3-chloro-6-(3,5-dichlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 147),
2-{4-[bis(4-fluorophenyl)methoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 148),
2-{4-(4-benzyloxyphenoxy)-2-chlorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 149),
2-{4-(4-benzyloxyphenoxy)-2-trifluoromethylphenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 150),
2-{4- [3-chloro-6- (2-trifluoromethylphenyl) benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 151),
2-{4-[(2R)-2-amino-2-phenylethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 152),
2-[4-(2-biphenylyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 153),
2-[4-(3-biphenylyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 154),
2-{4-[2-{(1-tert-butoxycarbonyl-4-piperidyl)methoxy}phenoxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 155),
2-{4-[3-{(1-tert-butoxycarbonyl-4-piperidyl)methoxy}phenoxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 156),
2-{4-[3-chloro-6- (3,4,5-trimethoxyphenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 157),
2-{4-[2-(2-biphenylyl)ethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 158),
2-[4-(2-biphenylylmethoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 159),

1-cyclohexyl-2-{4-[2-(4-piperidylmethoxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid hydrochloride (Example 160),
1-cyclohexyl-2-{4-[3-(4-piperidylmethoxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid hydrochloride (Example 161),
2-{4-[(2R)-2-acetylamino-2-phenylethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 162),
1-cyclohexyl-2-{4-[3-(4-methyl-3-pentenyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 163),
1-cyclohexyl-2-{4-[3-(3-methyl-3-butenyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 164),
2-{4-[{(2S)-1-benzyl-2-pyrrolidinyl}methoxy]phenyl}-1-cyclohexyl-benzimidazole-5-carboxylic acid hydrochloride (Example 165),
2-{4-[3-chloro-6-(4-methylthiophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 166),
2-{4-[3-chloro-6-(4-methanesulfonylphenyl)benzyloxy)phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 167),
2-{4-[3-chloro-6-(2-thienyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 168),
2-{4-[3-chloro-6-(3-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 169),
2-{4-[3-chloro-6-(3-pyridyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 170),
2-{4-[3-chloro-6-(4-fluorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 171),
2-[4-(4-benzyloxyphenoxy)-3-fluorophenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 172),
2-[4-(2-bromo-5-chlorobenzyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 173),
2-{4-[3-chloro-6-(4-chlorophenyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 174),
2-{4-[2-{(1-acetyl-4-piperidyl)methoxy}phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 175),
2-{4-[3-{(1-acetyl-4-piperidyl)methoxy}phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 176),
1-cyclohexyl-2-{4-[3-(2-propynyloxy)phenoxy]phenyl}benzimidazole-5-carboxylic acid (Example 177),
1-cyclohexyl-2-{4-[3-(3-pyridylmethoxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 178),
2-(4-benzyloxy-2-methoxyphenyl)-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 179),
2-[4-(2-bromo-5-methoxybenzyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 180),
2-[4-(carboxydiphenylmethoxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 181),
2-{4-[2-(4-chlorophenyl)-5-nitrobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 182),
2-{4-[3-acetylamino-6-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 183),
2-{4-[2-(4-carboxyphenyl)-5-chlorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 184),
2-{4-[{(2S)-1-benzyloxycarbonyl-2-pyrrolidinyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 185),
2-{2-chloro-4-[2-(4-trifluoromethylphenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 186),
1-cyclohexyl-2-{4- [3- (2-pyridylmethoxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 187),
2-{4-[2-(4-chlorophenyl)-5-fluorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 188),
2-{4-[3-carboxy-6-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 189),
2-{4-[3-carbamoyl-6-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 190),
1-cyclohexyl-2-{4-[2-(dimethylcarbamoylmethoxy)phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 191),
1-cyclohexyl-2-{4-[2-(piperidinocarbonylmethoxy)phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 192),
2-{4-[{(2S)-1-benzenesulfonyl-2-pyrrolidinyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 193),

2-{4-[{(2S)-1-benzoyl-2-pyrrolidinyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 194),
2-{4-[2-(4-carbamoylphenyl)-5-chlorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 195),
1-cyclohexyl-2-{4-[3-(dimethylcarbamoylmethoxy)phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 196),
1-cyclohexyl-2-{4-[3-(piperidinocarbonylmethoxy)phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 197),
1-cyclohexyl-2-{4-[3-{(1-methanesulfonyl-4-piperidyl)methoxy}-phenoxy]phenyl}benzimidazole-5-carboxylic acid (Example 198),
1-cyclohexyl-2-{4-[{2-methyl-5-(4-chlorophenyl) -4-oxazolyl}-methoxy]phenyl}benzimidazole-5-carboxylic acid (Example 199),
2-{4-[3-(3-chlorobenzyloxy)phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 200),
2-{4-[3-(4-chlorobenzyloxy)phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 201),
1-cyclohexyl-2-{4-[3-(4-fluorobenzyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 202),
1-cyclohexyl-2-(4-[{(2S)-1- (4-nitrophenyl) -2-pyrrolidinyl)-methoxy]phenyl}benzimidazole-5-carboxylic acid (Example 203),
1-cyclohexyl-2-{4-[{(2S) -1-phenyl-2-pyrrolidinyl}methoxy]-phenyl}benzimidazole-5-carboxylic acid hydrochloride (Example 204),
2-{4-[{(2S)-1-(4-acetylaminophenyl)-2-pyrrolidinyl}methoxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 205),
2-{4-[{5-(4-chlorophenyl)-2-methyl-4-thiazolyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 206),
2-{4-[bis(3-fluorophenyl)methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 207),
1-cyclohexyl-2-{4-[2-(4-chlorophenyl)-3-nitrobenzyloxy]phenyl}-benzimidazole-5-carboxylic acid (Example 208),
1-cyclohexyl-2-{4-[3-(4-tetrahydropyranyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 209),
1-cyclohexyl-2-{4-[3-(4-trifluoromethylbenzyloxy)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 210),
1-cyclohexyl-2-{4-[3-{(1-methyl-4-piperidyl)methoxy}phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 211),
2-{4-[3-(4-tert-butylbenzyloxy)phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 212),
2-{4-[3-(2-chlorobenzyloxy)phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 213),
1-cyclohexyl-2-{4-[3-(3-pyridyl)phenoxy]phenyl}benzimidazole-5-carboxylic acid (Example 214),
2-{4-[3- (4-chlorophenyl) phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 215),
1-cyclohexyl-2-{4-[3-(4-methoxyphenyl)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 216),
1-cyclohexyl-2-{4-[{4-(4-methanesulfonylphenyl)-2-methyl-5-thiazolylyl}methoxy]phenyl}benzimidazole-5-carboxylic acid (Example 217),
2-{4-[{4-(4-chlorophenyl)-2-methyl-5-thiazolyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 218),
2-{4-[1-(4-chlorobenzyl)-3-piperidyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 219),
1-cyclohexyl-2-{4-[3-{(2-methyl-4-thiazolyl)methoxy}phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 220),
1-cyclohexyl-2-{4-[3-{(2,4-dimethyl-5-thiazolyl)methoxy}phenoxy]-phenyl}benzimidazole-5-carboxylic acid (Example 221),
1-cyclohexyl-2-{4-[3-(3,5-dichlorophenyl)phenoxy]phenyl}-benzimidazole-5-carboxylic acid (Example 222),
2-{4-[1-(4-chlorobenzyl)-4-piperidyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 223),
2-{4-[3-(4-chlorobenzyloxy)piperidino]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 224),
2-{4-[4-carbamoyl-2-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 225),
2-{4-[4-(4-chlorobenzyloxy)piperidino]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 226),
2-{4-[3-{(2-chloro-4-pyridyl)methoxy}phenoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 227),
2-{4-[{(2S)-1-(4-dimethylcarbamoylphenyl) -2-pyrrolidinyl}-methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 228),
2-{4-[2- (4-chlorophenyl) -5-ethoxycarbonylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 229),

1-cyclohexyl-2-[4-(3-trifluoromethylphenoxy)phenyl]benzimidazole-5-carboxylic acid (Example 230),
1-cyclohexyl-2-{4-[{4-(4-dimethylcarbamoylphenyl)-2-methyl-5-thiazolyl}methoxy]phenyl}benzimidazole-5-carboxylic acid (Example 231),
2-{4-[2-(4-chlorophenyl)-5-dimethylcarbamoylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 232),
2-{4-[{4-(4-chlorophenyl)-2-methyl-5-pyrimidinyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 233),
2-{4-[{2-(4-chlorophenyl)-3-pyridyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid dihydrochloride (Example 234),
2-{4-[{3-(4-chlorophenyl)-2-pyridyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 235),
2-{4-[2-(3-chlorophenyl)-4-methylamino-1,3,5-triazin-6-yloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid trifluoroacetate (Example 236),
2-{4-[2-(4-chlorophenyl)-4-(5-tetrazolyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 237),
2-[4-(4-benzyloxy-6-pyrimidinyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 238),
1-cyclohexyl-2-{4-[4-(4-pyridylmethoxy)-6-pyrimidinyloxy]phenyl}-benzimidazole-5-carboxylic acid (Example 239),
2-{4-[4-(3-chlorophenyl)-6-pyrimidinyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 240),
methyl 2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 241),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexyl-benzimidazole-5-carboxylic acid hydrochloride (Example 242),
ethyl 2-{4-[3-(4-chlorophenyl)pyridin-2-ylmethoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 243),
methyl 2-[4-(2-bromo-5-tert-butoxycarbonylbenzyloxy)phenyl]-1-cyclohexylbenzimidazole-5-carboxylate (Example 244),
methyl 2-{4-[5-tert-butoxycarbonyl-2-(4-chlorophenyl)benzyloxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 245),
methyl 2-{4-[5-carboxy-2-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylate hydrochloride (Example 246),
methyl 2-{4-[2-(4-chlorophenyl)-5-methylcarbamoylbenzyloxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 247),
2-{4-[2-(4-chlorophenyl)-5-methylcarbamoylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 248),
2-{4-[3-(tert-butylsulfamoyl)-6-(4-chlorophenyl)benzyloxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 249),
2-{4-[2-(4-chlorophenyl)-5-sulfamoylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid trifluoroacetate (Example 250),
2-(4-benzyloxycyclohexyl)-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 251),
2-[2-(2-biphenylyloxymethyl)-5-thienyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 252),
2-[2-(2-biphenylyloxymethyl)-5-furyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 253),
1-cyclohexyl-2-{4-[{4- (4-fluorophenyl) -2-hydroxymethyl-5-thiazolyl}methoxy]phenyl}benzimidazole-5-carboxylic acid (Example 254),
1-cyclohexyl-2-{4-[{4-(4-carboxyphenyl)-2-methyl-5-thiazolyl}-methoxy]phenyl}benzimidazole-5-carboxylic acid hydrochloride (Example 255),
1-cyclohexyl-2-{2-fluoro-4-[4-fluoro-2-(3-fluorobenzoyl)-benzyloxy]phenyl}benzimidazole-5-carboxylic acid (Example 256),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-sulfonic acid (Example 257),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-3-cyclohexylbenzimidazole-4-carboxylic acid (Example 258),
1-cyclohexyl-2-{4-[3-dimethylcarbamoyl-5-(4-pyridylmethoxy)-phenoxy]phenyl}benzimidazole-5-carboxylic acid dihydrochloride (Example 259),
1-cyclohexyl-2-{4-[3-carboxy-5-(4-pyridylmethoxy)phenoxy]-phenyl}benzimidazole-5-carboxylic acid dihydrochloride (Example 260),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexylbenzimidazole-4-carboxylic acid (Exam-

ple 261),
2-{4-[3-carbamoyl-6-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 262),
2-{4-[{2-(4-carboxyphenyl)-3-pyridyl}methoxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 263),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-(4-tetrahydrothiopyranyl)benzimidazole-5-carboxylic acid (Example 264),
2-{4-[2-(4-chlorophenyl)-5-dimethylcarbamoylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 265),
1-cyclohexyl-2-{4-[3-dimethylcarbamoyl-6-(4-trifluoromethylphenyl)benzyloxy]phenyl}benzimidazole-5-carboxylic acid hydrochloride (Example 266),
1-cyclohexyl-2-{4-[3-dimethylcarbamoyl-6-(4-methylthiophenyl)-benzyloxy]phenyl}benzimidazole-5-carboxylic acid hydrochloride (Example 267),
2-{4-[2-(4-chlorophenyl)-5-methylcarbamoylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 268),
2-{4-[2-(4-chlorophenyl)-5-dimethylcarbamoylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 269),
2-{4-[3-carbamoyl-6-(4-chlorophenyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 270),
2-{4-[3-dimethylcarbamoyl-6-(4-methanesulfonylphenyl)benzyloxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 271),
2-{4-[3-dimethylcarbamoyl-6-(3-pyridyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid dihydrochloride (Example 272),
2-{4-[3-dimethylcarbamoyl-6-(4-dimethylcarbamoylphenyl)-benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 273),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-(1-oxo-4-tetrahydrothiopyranyl)benzimidazole-5-carboxylic acid (Example 274),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-(1,1-dioxo-4-tetrahydrothiopyranyl)benzimidazole-5-carboxylic acid (Example 275),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]-2-fluorophenyl}-1-(4-tetrahydrothiopyranyl)benzimidazole-5-carboxylic acid (Example 276),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]-2-fluorophenyl}-1-(l-oxo-4-tetrahydrothiopyranyl)benzimidazole-5-carboxylic acid (Example 277),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]-2-fluorophenyl}-1-(1,1-dioxo-4-tetrahydrothiopyranyl)benzimidazole-5-carboxylic acid (Example 278),
2-{4-[2-(4-chlorophenyl)-5-dimethylsulfamoylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 279),
2-{4-[2-(4-chlorophenyl)-5-methanesulfonylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 280),
methyl 2-{4-[5-carboxy-2-(4-chlorophenyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylate hydrochloride (Example 281),
2-{4-[2-(4-chlorophenyl)-5-dimethylaminobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid dihydrochloride (Example 282),
2-{4-[2-(4-chlorophenyl)-5-methanesulfonylaminobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 283),
2-{4-[2-(4-chlorophenyl)-5-diethylcarbamoylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 284),
2-{4-[2-(4-chlorophenyl)-5-isopropylcarbamoylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 285),
2-{4-[2-(4-chlorophenyl)-5-piperidinocarbonylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 286),
2-{4-[2-(4-chlorophenyl)-5-(1-pyrrolidinyl)carbonylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 287),
2-{4- [2-(4-chlorophenyl)-5- (2-hydroxyethyl)carbamoylbenzyloxy] -2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 288),
2-{4-[2-(4-chlorophenyl)-5-(4-hydroxypiperidino)-carbonylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 289),
2-{4-[2-(4-chlorophenyl)-5-morpholinocarbonylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-car-

boxylic acid hydrochloride (Example 290),
2-{4-[2-(4-chlorophenyl)-5-thiomorpholinocarbonylbenzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 291),
2-{4-[3-(carboxymethylcarbamoyl)-6-(4-chlorophenyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 292),
2-{4-[2-{4-(2-carboxyethyl) phenyl}-5-chlorobenzyloxy] phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 293),
2-{4-[3-chloro-6-(4-hydroxymethylphenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 294),
2-{4-[3-chloro-6-(4-methoxymethylphenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 295),
2-{4-[2-(3-carboxyphenyl)-5-chlorobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 296),
2-{4-[2-(4-chlorophenyl)-5-methylthiobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 297),
2-{4-[2-(4-chlorophenyl)-5-methylsulfinylbenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 298),
2-{4-[2-(4-chlorophenyl)-5-cyanobenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 299),
2-{4-[bis(3-pyridyl)methoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 300),
2-{4-[bis(4-dimethylcarbamoylphenyl)methoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 301),
sodium 2-{4-[2-thienyl-3-thienylmethoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 302),
methyl 2-{4-[2-(4-chlorophenyl)-5-(dimethylcarbamoyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 303),
sodium 2-{4-[2-(4-chlorophenyl)-5-(dimethylcarbamoyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 304),
2-{4-[5-carboxy-2-(4-chlorophenyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 305),
2-{4-[2-(4-carboxyphenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 306),
2-{4-[2-(4-carbamoylphenyl)-5-(dimethylcarbamoyl)benzyloxy]-phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 307),
2-{4-[5-amino-2-(4-chlorophenyl)benzyloxy]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 308),
2-{4-[5-(4-chlorophenyl)-2-methoxybenzylsulfinyl]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 309),
2-{4-[5-(4-chlorophenyl)-2-methoxybenzylsulfonyl]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 310),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzylthio]phenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 311),
2-{4-[bis(4-carboxyphenyl)methoxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 312),
2-[4-(phenyl-3-pyridylmethoxy)-2-fluorophenyl]-1-cyclohexylbenzimidazole-5-carboxylic acid (Example 313),
methyl 2-{4-[2-(4-chlorophenyl)-5-(methylcarbamoyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylate (Example 314),
2-{4-[5-chloro-2-(4-pyridyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 315),
2-{4-[2-(4-chlorophenyl)-5-(benzylcarbamoyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 316),
2-{4-[2-(4-chlorophenyl)-5-(cyclohexylmethylcarbamoyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 317),
2-{4-[2-(4-chlorophenyl)-5-(4-pyridylmethylcarbamoyl)benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid dihydrochloride (Example 318),
2-{4-[2- (4-chlorophenyl) -5- (N-benzyl-N-methylcarbamoyl)-benzyloxy]-2-fluorophenyl}-1-cyclohexylbenzimidazole-5-carboxylic acid hydrochloride (Example 319),
methyl 2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexyl-1H-indole-5-carboxylate (Exam-

ple 501),
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-1-cyclohexyl-1H-indole-5-carboxylic acid (Example 502),
2-(4-benzyloxyphenyl)-1-cyclopentyl-lH-indole-5-carboxylic acid (Example 503),
ethyl 2-(4-benzyloxyphenyl)-3-cyclohexylimidazo[1,2-a]pyridine-7-carboxylate (Example 601),
2-(4-benzyloxyphenyl)-3-cyclohexylimidazo[1,2-a]pyridine-7-carboxylic acid (Example 602), and
2-{4-[2-(4-chlorophenyl)-5-methoxybenzyloxy]phenyl}-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (Example 701).

(32) A pharmaceutical composition comprising a fused ring compound of any of (14) to (31) above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
(33) A hepatitis C virus polymerase inhibitor comprising a fused ring compound of any of (1) to (31) above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
(34) An anti-hepatitis C virus agent comprising a fused ring compound of any of (1) to (31) above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
(35) A therapeutic agent for hepatitis C comprising a fused ring compound of any of (14) to (31) above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
(36) A method for treating hepatitis C, which comprises administering an effective amount of a fused ring compound of the above-mentioned formula [I] or a pharmaceutically acceptable salt thereof.
(37) A method for inhibiting hepatitis C virus polymerase, which comprises administering an effective amount of a fused ring compound of the above-mentioned formula [I] or a pharmaceutically acceptable salt thereof.
(38) Use of a fused ring compound of the above-mentioned formula [I] or a pharmaceutically acceptable salt thereof for the production of a pharmaceutical agent for treating hepatitis C.
(39) Use of a fused ring compound of the above-mentioned formula [I] or a pharmaceutically acceptable salt thereof for the production of a hepatitis C virus polymerase inhibitor.
(40) A pharmaceutical composition for the treatment of hepatitis C, which comprises a fused ring compound of the above-mentioned formula [I] or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
(41) A pharmaceutical composition for inhibiting hepatitis C virus polymerase, which comprises a fused ring compound of the above-mentioned formula [I] or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
(42) A commercial package comprising a pharmaceutical composition of (40) above and a written matter associated therewith, the written matter stating that the pharmaceutical composition can or should be used for treating hepatitis C.
(43) A commercial package comprising a pharmaceutical composition of (41) above and a written matter associated therewith, the written matter stating that the pharmaceutical composition can or should be used for inhibiting hepatitis C virus polymerase.

[0033] The definitions of respective substituents and moieties used in the present specification are as follows.
[0034] The halogen atom is a fluorine atom, chlorine atom, bromine atom or iodine atom, preferably fluorine atom, chlorine atom or bromine atom.
[0035] Particularly preferably, the halogen atom is fluorine atom at R^5, $R^{5'}$, R^6, $R^{6'}$, group A and group C, and fluorine atom or chlorine atom at X, Z, Z', group B and group D.
[0036] The C_{1-6} alkyl is straight chain or branched chain alkyl having 1 to 6 carbon atoms, and is exemplified by methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, tert-pentyl, hexyl and the like.
[0037] Preferably, it is straight chain or branched chain alkyl having 1 to 4 carbon atoms, and is particularly preferably methyl at R^{a7}, R^{a8}, R^{a9}, R^{a15}, R^{a16}, R^{a17}, R^{a29}, R^{a33}, R^{b6} and R^{b7} and methyl or tert-butyl at R^{b1}, R^{b2}, group B and group C.
[0038] The halogenated C_{1-6} alkyl is the above-defined C_{1-6} alkyl except that it is substituted by the above-defined halogen atom. Preferably, it is halogenated alkyl wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include fluoromethyl, difluoromethyl, trifluoromethyl, bromomethyl, chloromethyl, 1,2-dichloromethyl, 2,2-dichloromethyl, 2,2,2-trifluoroethyl and the like.
[0039] The halogenated C_{1-6} alkyl is particularly preferably trifluoromethyl at group B.
[0040] The C_{1-6} alkylene is straight chain alkylene having 1 to 6 carbon atoms, and is exemplified by methylene, ethylene, trimethylene, tetramethylene, pentamethylene or hexamethylene.
[0041] The C_{1-6} alkylene is preferably methylene or ethylene at Y.
[0042] The C_{2-6} alkenylene is straight chain alkenylene having 2 to 6 carbon atoms, and is exemplified by vinylene, propenylene, 1-butenylene, 1,3-butadienylene and the like.

[0043] The C_{2-6} alkenylene is preferably vinylene at Y.

[0044] The C_{1-6} alkoxy is alkyloxy wherein the alkyl moiety thereof is the above-defined C_{1-6} alkyl. Preferably, it is alkoxy wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include methoxy, ethoxy, propoxy, isopropyloxy, butoxy, isobutyloxy, tert-butyloxy, pentyloxy, hexyloxy and the like.

[0045] The C_{1-6} alkoxy is particularly preferably methoxy at R^{a2}, R^{a3}, group A and group C.

[0046] The C_{1-6} alkanoyl is alkylcarbonyl wherein the alkyl moiety thereof is the above-defined C_{1-6} alkyl. Preferably, it is alkanoyl wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include acetyl, propionyl, butyryl, isobutyryl, pivaloyl and the like.

[0047] The C_{1-6} alkanoyl is particularly preferably acetyl at R^1, R^2, R^3, R^4, R^{a5}, R^{a29}, R^{b7} and group B.

[0048] The C_{1-6} alkoxycarbonyl is alkyloxycarbonyl wherein the alkoxy moiety thereof is the above-defined C_{1-6} alkoxy. Preferably, it is alkoxycarbonyl wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropyloxycarbonyl, butoxycarbonyl, isobutyloxycarbonyl, tert-butyloxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl and the like.

[0049] The C_{1-6} alkoxycarbonyl is particularly preferably methoxycarbonyl or ethoxycarbonyl at R^{a10} and group A.

[0050] The C_{1-6} alkylamino is alkylamino or dialkylamino wherein the alkyl moiety thereof is the above-defined C_{1-6} alkyl. Preferably, it is alkylamino or dialkylamino wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include methylamino, ethylamino, propylamino, isopropylamino, butylamino, isobutylamino, tert-butylamino, pentylamino, hexylamino, dimethylamino, diethylamino, methylethylamino, N-isopropyl-N-isobutylamino and the like.

[0051] The C_{1-6} alkylamino is particularly preferably methylamino at R^{a7}, and particularly preferably dimethylamino at R^{a21} and group A.

[0052] The C_{1-6} alkanoylamino is alkylcarbonylamino wherein the alkanoyl moiety thereof is the above-defined C_{1-6} alkanoyl. Preferably, it is alkylcarbonylamino wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include acetylamino, propionylamino, butyrylamino, isobutyrylamino, pivaloylamino and the like.

[0053] The C_{1-6} alkanoylamino is particularly preferably acetylamino at X and R^{a10}.

[0054] The C_{1-6} alkylsulfonyl is alkylsulfonyl wherein the alkyl moiety thereof is the above-defined C_{1-6} alkyl. Preferably, it is alkylsulfonyl wherein the alkyl moiety thereof is straight chain or branched chain alkyl having 1 to 4 carbon atoms. Examples thereof include methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl, butylsulfonyl, isobutylsulfonyl, tertbutylsulfonyl, pentylsulfonyl, hexylsulfonyl and the like.

[0055] The C_{1-6} alkylsulfonyl is particularly preferably methylsulfonyl at X and R^{a5}.

[0056] The C_{6-14} aryl is aromatic hydrocarbon having 6 to 14 carbon atoms. Examples thereof include phenyl, naphthyl, anthryl, indenyl, azulenyl, fluorenyl, phenanthryl and the like.

[0057] The C_{6-14} aryl is preferably phenyl or naphthyl, particularly preferably phenyl at the ring A, ring A', ring B and ring B'.

[0058] The C_{3-8} cycloalkyl is saturated cycloalkyl having 3 to 8, preferably 5 to 7, carbon atoms. Examples thereof include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

[0059] The C_{3-8} cycloalkyl is particularly preferably cyclohexyl at the ring A, ring A', ring B and ring B'.

[0060] The C_{3-8} cycloalkenyl is cycloalkenyl having 3 to 8, preferably 5 to 7, carbon atoms and has at least 1, preferably 1 or 2, double bond(s). Examples thereof include cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentadienyl, cyclohexenyl, 2,4-cyclohexadien-1-yl, 2,5-cyclohexadien-1-yl, cycloheptenyl and cyclooctenyl and the like, but do not include aryl (e.g., phenyl) or completely saturated cycloalkyl.

[0061] The C_{3-8} cycloalkenyl is preferably cyclohexenyl at the ring A and ring A'.

[0062] The heterocyclic group has, as an atom constituting the ring, 1 to 4 heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom, besides a carbon atom, and includes saturated ring and unsaturated ring, monocyclic ring and fused ring having the number of ring atom constituting the ring of 3 to 14.

[0063] The heterocyclic group as a monocyclic ring includes, for example, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyrrolinyl, pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyranyl and the like.

[0064] Examples of the heterocyclic group as a fused ring include quinolyl, isoquinolyl, quinazolinyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, 5,6,7,8-tetrahydroquinolyl, indolyl, benzimidazolyl, indolinyl, benzofuranyl, benzothienyl, benzoxazolyl, benzothiazolyl and the like.

[0065] Preferably, it is a heterocyclic group which is a 5-membered or a 6-membered monocyclic group. Examples thereof include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyrrolidinyl, piperidyl, piperazinyl and the like.

[0066] The heterocyclic group is preferably pyridyl, pyrazinyl, pyrimidinyl or pyridazinyl which is an aromatic group, and particularly preferably pyridyl at the ring A and ring A'.

[0067] The heterocyclic group is particularly preferably pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl or thiadiazolyl, which is an aromatic group, at the ring B and ring B'. More preferably it is pyridyl or thiazolyl, most preferably thiazolyl.

[0068] The C_{6-14} aryl C_{1-6} alkyl is arylalkyl wherein the alkyl moiety thereof is the above-defined C_{1-6} alkyl and the aryl moiety is the above-defined C_{6-14} aryl. Preferably, it is arylalkyl wherein the alkyl moiety thereof is straight chain alkyl having 1 to 4 carbon atoms and the aryl moiety is phenyl. Examples thereof include benzyl, phenethyl, 3-phenylpropyl, 2-phenylpropyl, 4-phenylbutyl and the like.

[0069] The C_{6-14} aryl C_{1-6} alkyl is particularly preferably benzyl at R^{a8} and R^{b6}.

[0070] The C_{6-14} aryl C_{1-6} alkyloxycarbonyl is arylalkyloxycarbonyl wherein the C_{6-14} aryl C_{1-6} alkyl moiety thereof is the above-defined C_{6-14} aryl C_{1-6} alkyl. Preferably, it is arylalkyloxycarbonyl wherein the alkyl moiety thereof is straight chain alkyl having 1 to 4 carbon atoms and the aryl moiety is phenyl. Examples thereof include benzyloxycarbonyl, phenethyloxycarbonyl, 3-phenylpropyloxycarbonyl, 2-phenylpropyloxycarbonyl, 4-phenylbutyloxycarbonyl and the like.

[0071] The C_{6-14} aryl C_{1-6} alkyloxycarbonyl is particularly preferably benzyloxycarbonyl at R^{b7}.

[0072] The optionally substituted C_{1-6} alkyl is the above-defined C_{1-6} alkyl, preferably that wherein straight chain or branched chain alkyl having 1 to 4 carbon atoms is optionally substituted with 1 to 3 substituent(s), and includes unsubstituted alkyl. The substituent(s) is(are) selected from the above-defined halogen atom, hydroxyl group, carboxyl, amino, the above-defined C_{1-6} alkoxy, the above-defined C_{1-6} alkoxycarbonyl and the above-defined C_{1-6} alkylamino. Examples of optionally substituted C_{1-6} alkyl include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, tert-pentyl, neopentyl, 1-ethylpropyl, hexyl, trifluoromethyl, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl, 4-hydroxybutyl, 1-hydroxy-1-methylethyl, carboxylmethyl, 2-carboxylethyl, methoxymethyl, ethoxycarbonylmethyl, 2-ethoxycarbonylethyl, 2-dimethylaminoethyl and the like.

[0073] Preferably, the optionally substituted C_{1-6} alkyl is methyl, 1-hydroxy-1-methylethyl, carboxylmethyl or 2-dimethylaminoethyl at R^1, R^2, R^3 and R^4, methyl or trifluoromethyl at R^5, $R^{5'}$, R^6 and $R^{6'}$, methyl at R^7, R^8, R^{a18}, R^{a24}, R^{a25}, R^{a31} and R^{b5}, methyl or ethyl at R^{a1} and R^{a19}, methyl, carboxylmethyl or 2-dimethylaminoethyl at R^{a2} and R^{a3}, methyl or carboxylmethyl at R^{a6}, methyl, ethyl, isopropyl, butyl or trifluoromethyl at X, methyl, ethyl, isopropyl, butyl, isobutyl, tert-butyl, isopentyl, neopentyl, 1-ethylpropyl or carboxylmethyl at R^{a10}, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, trifluoromethyl, 2-hydroxyethyl or carboxylmethyl at R^{a11}, methyl or 4-hydroxybutyl at R^{a12}, methyl, ethyl, isopropyl, butyl, 2-hydroxyethyl, 4-hydroxybutyl, ethoxycarbonylmethyl, 2-(ethoxycarbonyl)ethyl or 2-dimethylaminoethyl at R^{a13}, methyl, propyl, butyl, isopentyl, trifluoromethyl, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl or carboxymethyl at R^{a20}, methyl or ethyl at R^{a22} and R^{a23}, methyl or tert-butyl at R^{a26}, methyl, ethyl, isopropyl, 2-hydroxyethyl or carboxylmethyl at R^{a27} and R^{a28}, and methyl, ethyl, propyl, isopropyl, tert-butyl, trifluoromethyl, hydroxymethyl, 2-hydroxyethyl, 2-carboxylethyl, methoxymethyl or ethoxycarbonylmethyl at Z, Z' and group D.

[0074] It is particularly preferably, trifluoromethyl at R^5, $R^{5'}$, R^6 and $R^{6'}$, methyl or tert-butyl at R^{a26}, methyl, tert-butyl, trifluoromethyl or hydroxymethyl at Z, Z' and group D, and methyl at other substituents.

[0075] The optionally substituted C_{2-6} alkenyl is that wherein straight chain or branched chain alkenyl having 2 to 6 carbon atoms is optionally substituted by 1 to 3 substituent(s), and includes unsubstituted alkenyl. The substituent(s) is(are) selected from the above-defined halogen atom, hydroxyl group, carboxyl, amino, the above-defined C_{1-6} alkoxy, the above-defined C_{1-6} alkoxycarbonyl and the above-defined C_{1-6} alkylamino. Examples of optionally substituted C_{2-6} alkenyl include vinyl, allyl, 1-propenyl, isopropenyl, 1-butenyl, 2-butenyl, 1,3-butadienyl, 2-isopentenyl, 3-isohexenyl, 4-methyl-3-pentenyl, 2-carboxylethenyl and the like.

[0076] The optionally substituted C_{2-6} alkenyl is preferably 2-carboxylethenyl at X, and preferably 2-isopentenyl, 3-isohexenyl or 4-methyl-3-pentenyl at R^{a20}.

[0077] The optionally substituted C_{2-6} alkynyl is that wherein straight chain or branched chain alkynyl having 2 to 6 carbon atoms is optionally substituted by 1 to 3 substituent(s), and includes unsubstituted alkynyl. The substituent(s) is(are) selected from the above-defined halogen atom, hydroxyl group, carboxyl, amino, the above-defined C_{1-6} alkoxy, the above-defined C_{1-6} alkoxycarbonyl and the above-defined C_{1-6} alkylamino. Examples thereof include ethynyl, 1-propynyl, 2-propynyl, 3-butynyl and the like.

[0078] The optionally substituted C_{2-6} alkynyl is preferably 2-propynyl at R^{a20}.

[0079] The C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group B is that wherein the above-defined C_{6-14} aryl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted aryl. The substituent(s) is(are) selected from the above-defined halogen atom, cyano, nitro, the above-defined C_{1-6} alkyl, the above-defined halogenated C_{1-6} alkyl, the above-defined C_{1-6} alkanoyl, $-(CH_2)_r-COOR^{b1}$, $-(CH_2)_r-CONR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}-COR^{b2}$, $-(CH_2)_r-NHSO_2R^{b1}$, $-(CH_2)_r-OR^{b1}$, $-(CH_2)_r-SR^{b1}$, $-(CH_2)_r-SO_2R^{b1}$ and $-(CH_2)_r-SO_2NR^{b1}R^{b2}$ (wherein R^{b1} and R^{b2} are each independently hydrogen atom or the above-defined C_{1-6} alkyl and r is 0 or an integer of 1 to 6).

[0080] Examples thereof include phenyl, naphthyl, anthryl, indenyl, azulenyl, fluorenyl, phenanthryl, 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,4-dichlorophenyl, 3,5-dichlorophenyl, pentafluorophenyl, 4-methylphenyl, 4-tert-butylphenyl, 2-trifluoromethylphenyl, 4-trifluoromethylphenyl, 4-nitrophenyl, 4-cyanophenyl, 4-acetylphenyl, 4-carboxylphenyl, 4-carbamoylphenyl, 4-aminophenyl, 4-dimethylaminophenyl, 4-acetylaminophenyl, 4-(methylsulfonylamino)phenyl, 4-methoxyphenyl, 3,4,5-trimethoxyphenyl, 4-methylthiophenyl, 4-methylsulfonylphenyl, 4-aminosulfonylphenyl, 3-nitro-4-methoxyphenyl and 4-nitro-3-methoxyphenyl.

[0081] The aryl moiety is preferably phenyl, the group B here is preferably the above-defined halogen atom, nitro, the above-defined C_{1-6} alkyl, the above-defined halogenated C_{1-6} alkyl or $-(CH_2)_r-OR^{b1}$. Examples of group B include fluorine atom, chlorine atom, nitro, methyl, tert-butyl, trifluoromethyl and methoxy. Particularly preferably, it is fluorine atom or chlorine atom.

[0082] With regard to "C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group B", it is preferably phenyl, 4-tert-butylphenyl, 3-chlorophenyl, 4-chlorophenyl, 4-methoxyphenyl or 4-trifluoromethylphenyl at R^{a12}, R^{a27} and R^{a28}, phenyl at R^{a14}, R^{a22}, R^{a23}, R^{a26} and R^{b5}, phenyl or 3-fluorophenyl at R^{a18}, phenyl or 2,4-dichlorophenyl at R^{a20}, phenyl, 4-chlorophenyl, 4-trifluoromethylphenyl, 3,5-dichlorophenyl, 3-nitro-4-methoxyphenyl or 4-nitro-3-methoxyphenyl at R^{a24}, and phenyl or 4-methylphenyl at R^{a25}.

[0083] It is particularly preferably phenyl at other substituents.

[0084] The C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D is that wherein the above-defined C_{6-14} aryl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted aryl. The substituent(s) is(are) selected from the above-mentioned group D (substituents shown under (a) to (p)).

[0085] Examples of group D here include fluorine atom, chlorine atom, bromine atom, nitro, cyano, methyl, ethyl, propyl, isopropyl, tert-butyl, trifluoromethyl, hydroxymethyl, 2-hydroxyethyl, methoxymethyl, 2-carboxylethyl, methoxycarbonylmethyl, ethoxycarbonylmethyl, acetyl, carboxyl, methoxycarbonyl, ethoxycarbonyl, carbamoyl, methylaminocarbonyl, isopropylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, (2-hydroxyethyl)aminocarbonyl, (carboxylmethyl)aminocarbonyl, hydroxyl group, methoxy, ethoxy, propyloxy, isopropyloxy, isopentyloxy, 2-isopentenyloxy, 3-isohexenyloxy, 4-methyl-3-pentenyloxy, 2-propynyloxy, hydroxymethyloxy, carboxylmethyloxy, (dimethylaminocarbonyl)methyloxy, amino, methylamino, dimethylamino, diethylamino, acetylamino, methylsulfonylamino, methylthio, methylsulfonyl, methylsulfinyl, aminosulfonyl, methylaminosulfonyl and dimethylaminosulfonyl.

[0086] Examples of C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D include phenyl, naphthyl, anthryl, indenyl, azulenyl, fluorenyl, phenanthryl, 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 4-bromophenyl, 4-nitrophenyl, pentafluorophenyl, 4-methylphenyl, 4-tert-butylphenyl, 2-trifluoromethylphenyl, 4-trifluoromethylphenyl, 4-(hydroxymethyl)phenyl, 4-(methoxymethyl)phenyl, 4-(2-carboxylethyl)phenyl, 3-carboxylphenyl, 4-carboxylphenyl, 4-methoxyphenyl, 3,4,5-trimethoxyphenyl, 4-carbamoylphenyl, 4-methylthiophenyl, 4-(dimethylaminocarbonyl)phenyl, 4-methylsulfonylphenyl, 4-acetylaminophenyl, 4-cyanophenyl, 4-acetylphenyl, 4-aminophenyl, 4-dimethylaminophenyl, 4-(methylsulfonylamino)phenyl, 4-methylsulfinylphenyl, 4-aminosulfonylphenyl and 3-nitro-4-methoxyphenyl and 4-nitro-3-methoxyphenyl.

[0087] At Z and Z', the aryl moiety is preferably phenyl, and group D here is preferably the above-defined halogen atom, nitro, the above-defined optionally substituted C_{1-6} alkyl, $-(CH_2)_t-COOR^{a19}$, $-(CH_2)_t-CONR^{a27}R^{a28}$, $-(CH_2)_t-OR^{a20}$, $-(CH_2)_t-NR^{a29}CO-R^{a24}$, $-(CH_2)_t-S(O)_q-R^{a25}$ or $-(CH_2)_t-SO_2-NHR^{a26}$.

[0088] Examples of C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D preferably include phenyl, 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,5-dichlorophenyl, 4-bromophenyl, 4-nitrophenyl, 4-methylphenyl, 4-tert-butylphenyl, 2-trifluoromethylphenyl, 4-trifluoromethylphenyl, 4-(hydroxymethyl)phenyl, 4-(methoxymethyl)phenyl, 4-(2-carboxylethyl)phenyl, 3-carboxylphenyl, 4-carboxylphenyl, 4-methoxyphenyl, 3,4,5-trimethoxyphenyl, 4-carbamoylphenyl, 4-methylthiophenyl, 4-(dimethylaminocarbonyl)phenyl, 4-methylsulfonylphenyl, 4-acetylaminophenyl, 4-methylsulfinylphenyl and 4-aminosulfonylphenyl.

[0089] Particularly preferably, it is the above-defined halogen atom, the above-defined optionally substituted C_{1-6} alkyl, $-(CH_2)_tCOOR^{a19}$, $-(CH_2)_t-CONR^{a27}R^{a28}$, $(CH_2)_t-OR^{a20}$ or $-(CH_2)_t-S(O)_q-R^{a25}$, which is specifically fluorine atom, chlorine atom, bromine atom, nitro, methyl, tert-butyl, carboxyl, trifluoromethyl, hydroxymethyl, methoxymethyl, 2-carboxylethyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl or acetylamino. More preferably, it is fluorine atom, chlorine atom, methyl, tert-butyl, carboxyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl or acetylamino, most preferably fluorine atom or chlorine atom.

[0090] The heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from group B is that wherein the above-defined heterocyclic group is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted heterocyclic group. The substituent(s) is(are) selected from the above-defined halogen atom, cyano, nitro, the above-defined C_{1-6} alkyl, the above-defined halogenated C_{1-6} alkyl, the above-defined C_{1-6} alkanoyl, $-(CH_2)_r-COOR^{b1}$, $-(CH_2)_r-CONR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}R^{b2}$, $-(CH_2)_r-NR^{b1}-COR^{b2}$, $-(CH_2)_r-NHSO_2R^{b1}$, $-(CH_2)_r-OR^{b1}$, $-(CH_2)_r-SR^{b1}$, $-(CH_2)_r-SO_2R^{b1}$ and $-(CH_2)_r-SO_2NR^{b1}R^{b2}$ wherein R^{b1} and R^{b2} are each independently hydrogen atom or the above-defined C_{1-6} alkyl and r is 0 or an integer of 1 to 6.

[0091] Examples thereof include 2-pyridyl, 3-pyridyl, 4-pyridyl, 3-fluoropyridin-4-yl, 3-chloropyridin-4-yl, 4-chloropy-

ridin-3-yl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, 2-thienyl, 3-thienyl, furyl, oxazolyl, 2-methyloxazol-4-yl, isoxazolyl, thiazolyl, 2-methylthiazol-4-yl, 2,5-dimethylthiazol-4-yl, 2,4-dimethylthiazol-5-yl, isothiazolyl, thiadiazolyl, pyrrolinyl, pyrrolidinyl, 3-hydroxypyrrolidinyl, imidazolidinyl, piperidyl, 3-hydroxypiperidino, 4-hydroxypiperidino, 3,4-dihydroxypiperidino, 4-methoxypiperidino, 4-carboxypiperidino, 4-(hydroxymethyl)-piperidino, 2-oxopiperidino, 4-oxopiperidino, 2,2,6,6-tetramethylpiperidino, 2,2,6,6-tetramethyl-4-hydroxypiperidino, N-methylpiperidin-4-yl, N-(tert-butoxycarbonyl)piperidin-4-yl, N-acetylpiperidin-4-yl, N-methylsulfonylpiperidin-4-yl, piperazinyl, 4-methylsulfonylpiperazinyl, morpholinyl, thiomorpholinyl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, tetrahydropyranyl, quinolyl, isoquinolyl, quinazolinyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, 5,6,7,8-tetrahydroquinolyl, indolyl, benzimidazolyl, indolinyl, benzofuranyl, benzothienyl, benzoxazolyl, benzothiazolyl and the like.

[0092] The heterocyclic moiety is preferably a heterocyclic group which is a 5-membered or a 6-membered monocyclic group. Examples thereof include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl and tetrahydropyranyl, and the group B here is preferably the above-defined halogen atom, the above-defined C_{1-6} alkyl, the above-defined halogenated C_{1-6} alkyl, the above-defined C_{1-6} alkanoyl, $-(CH_2)_r-COOR^{b1}$, $-(CH_2)_r-CONR^{b1}R^{b2}$ or $-(CH_2)_r-OR^{b1}$.

[0093] Examples of heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from group B preferably include piperidino, 4-hydroxypiperidino, 1-piperazinyl, 1-(methylsulfonyl)piperidin-4-yl, 1-pyrrolidinyl, morpholino, 4-thiomorpholinyl, tetrahydropyranyl, pyridyl and thiazolyl. Particularly preferably, it is piperidino, 4-hydroxypiperidino, 1-piperazinyl, 1-pyrrolidinyl, morpholino or 4-thiomorpholinyl at R^{a18}, tetrahydropyranyl or 4-hydroxypiperidino at R^{a20}, piperidino at R^{a21}, pyridyl at R^{a24} and R^{a25}, pyridyl or thiazolyl at R^{a26} and at R^{a27} and R^{a28}, it is 1-(methylsulfonyl)piperidin-4-yl, 3-hydroxypyrrolidinyl, 3-hydroxypiperidino, 4-hydroxypiperidino, 3,4-dihydroxypiperidino, 4-methoxypiperidino, 4-carboxypiperidino, 4-(hydroxymethyl)piperidino, 2-oxopiperidino, 4-oxopiperidino, 2,2,6,6-tetramethylpiperidino, 2,2,6,6-tetramethyl-4-hydroxypiperidino, 4-methylsulfonylpiperazinyl, 1-oxothiomorpholin-4-yl or 1,1-dioxothiomorpholin-4-yl.

[0094] The heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from group D is that wherein the above-defined heterocyclic group is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted heterocyclic group. The substituent(s) is(are) selected from the substituent(s) of the above-mentioned group D (substituents shown under (a) to (p)).

[0095] Examples of the group D here include the substituent(s) exemplified for C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D.

[0096] Examples of heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from group D include 2-pyridyl, 3-pyridyl, 4-pyridyl, 3-fluoropyridin-4-yl, 3-chloropyridin-4-yl, 4-chloropyridin-3-yl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, 2-thienyl, 3-thienyl, furyl, oxazolyl, 2-methyloxazol-4-yl, isoxazolyl, thiazolyl, 2-methylthiazol-4-yl, 2,5-dimethylthiazol-4-yl, 2,4-dimethylthiazol-5-yl, isothiazolyl, thiadiazolyl, pyrrolinyl, pyrrolidinyl, imidazolidinyl, piperidyl, N-methylpiperidin-4-yl, N-(tert-butoxycarbonyl)piperidin-4-yl, N-acetylpiperidin-4-yl, N-methylsulfonylpiperidin-4-yl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyranyl, quinolyl, isoquinolyl, quinazolinyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, 5,6,7,8-tetrahydroquinolyl, indolinyl, benzimidazolyl, indolinyl, benzofuranyl, benzothienyl, benzoxazolyl, benzothiazolyl and the like.

[0097] In addition, the heterocyclic group may be substituted at the 3-, 4-, 5- or 6-position of 2-pyridyl, at the 2-, 4-, 5- or 6-position of 3-pyridyl, at the 2-, 3-, 5- or 6-position of 4-pyridinyl, at the 3-, 4- or 5-position of 2-thienyl, or at the 2-, 4- or 5-position of 3-thienyl, by fluorine atom, chlorine atom, bromine atom, nitro, methyl, tert-butyl, carboxyl, trifluoromethyl, hydroxymethyl, methoxymethyl, 2-carboxylethyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl or acetylamino.

[0098] At Z and Z', the heterocyclic moiety is preferably a heterocyclic group which is a 5-membered or 6-membered monocyclic group. Examples thereof include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolinyl, thiadiazolyl, pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl and tetrahydropyranyl. The group D here is preferably the above-defined halogen atom, nitro, the above-defined optionally substituted C_{1-6} alkyl, $-(CH_2)_t-COOR^{a19}$, $-(CH_2)_t-CONR^{a27}R^{a28}$, $-(CH_2)_t-OR^{a20}$, $-(CH_2)_t-NR^{a29}CO-R^{a24}$, $-(CH_2)_t-S(O)_q-R^{a25}$ or $-(CH_2)_t-SO_2-NHR^{a26}$.

[0099] Examples of heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from group D preferably include piperidino, 4-hydroxypiperidino, 1-piperazinyl, 1-pyrrolidinyl, morpholino, 4-thiomorpholinyl, 4-tetrahydropyranyl, 3-pyridyl, 2-pyrimidinyl, 5-tetrazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl and 2-thienyl.

[0100] Particularly preferably, it is pyridyl, pyrimidinyl, tetrazolyl, thienyl or piperidyl.

[0101] The C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from group C is that wherein the above-defined C_{3-8} cycloalkyl is optionally substituted by the 1 to 5 substituent(s) selected from hydroxyl group, the above-defined halogen atom, the above-defined C_{1-6} alkyl and the above-defined C_{1-6} alkoxy, which may be unsubstituted. Examples thereof include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, 4fluorocyclohexyl,

2-methylcyclopentyl, 3-methylcyclohexyl, 4-methylcyclohexyl, 4,4-dimethylcyclohexyl, 3,5-dimethylcyclohexyl, 4-tert-butylcyclohexyl, 4-hydroxycyclohexyl, 4-methoxycyclohexyl and 2,3,4,5,6-pentafluorocyclohexyl.

[0102] The cycloalkyl moiety is preferably cyclopentyl or cyclohexyl, particularly preferably cyclohexyl.

[0103] At the ring Cy and ring Cy', the C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from group C is preferably cyclopentyl, cyclohexyl, 4-fluorocyclohexyl, 4-methylcyclohexyl, 4,4-dimethylcyclohexyl, 4-tert-butylcyclohexyl, 4-hydroxycyclohexyl or 4-methoxycyclohexyl, more preferably cyclopentyl or cyclohexyl, particularly preferably cyclohexyl.

[0104] The C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B is that wherein the above-defined C_{3-8} cycloalkyl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted cycloalkyl. The substituents are selected from the above group B.

[0105] Specific examples thereof include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, 4-fluorocyclohexyl, 2-methylcyclopentyl, 3-methylcyclohexyl, 4-methylcyclohexyl, 4,4-dimethylcyclohexyl, 3,5-dimethylcyclohexyl, 4-tert-butylcyclohexyl, 4-hydroxycyclohexyl, 4-methoxycyclohexyl and 2,3,4,5,6-pentafluorocyclohexyl.

[0106] Also exemplified are those wherein cyclopentyl or cyclohexyl is substituted by fluorine atom, chlorine atom, bromine atom, nitro, methyl, tert-butyl, carboxyl, trifluoromethyl, hydroxymethyl, methoxymethyl, 2-carboxylethyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl or acetylamino.

[0107] At cycloalkyl moiety, it is preferably cyclopentyl or cyclohexyl. As the C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B, it is particularly preferably cyclohexyl or 4-hydroxycyclohexyl at R^{a27} and R^{a28}.

[0108] The C_{3-8} cycloalkyl optionally substituted by 1 to 5 substituent(s) selected from group D is that wherein the above-defined C_{3-8} cycloalkyl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted cycloalkyl. The substituent(s) is(are) selected from the substituent(s) of the above-mentioned group D (substituents shown under (a) to (p)).

[0109] The group D here includes the substituents recited with regard to C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D.

[0110] Examples thereof include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, 4-fluorocyclohexyl, 2-methylcyclopentyl, 3-methylcyclohexyl, 4-methylcyclohexyl, 4,4-dimethylcyclohexyl, 3,5-dimethylcyclohexyl, 4-tert-butylcyclohexyl, 4-hydroxycyclohexyl, 4-methoxycyclohexyl and 2,3,4,5,6-pentafluorocyclohexyl.

[0111] The group D may be, for example, cyclopentyl or cyclohexyl substituted by fluorine atom, chlorine atom, bromine atom, nitro, methyl, tert-butyl, carboxyl, trifluoromethyl, hydroxymethyl, methoxymethyl, 2-carboxylethyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl or acetylamino.

[0112] The cycloalkyl moiety is preferably cyclopentyl or cyclohexyl, and at Z and Z', it is particularly preferably cyclohexyl.

[0113] The optionally substituted C_{3-8} cycloalkenyl is that wherein the above-defined C_{3-8} cycloalkenyl is optionally substituted by substituent(s) selected from hydroxyl group, the above-defined halogen atom, the above-defined C_{1-6} alkyl and the above-defined C_{1-6} alkoxy, which may be unsubstituted. Examples thereof include cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentadienyl, cyclohexenyl, 4-fluoro-2-cyclohexenyl, 4-methyl-2-cyclohexenyl, 4-methyl-3-cyclohexenyl, 2,4-cyclohexadien-1-yl, 2,5-cyclohexadien-1-yl, cycloheptenyl and cyclooctenyl and the like, but do not include aryl (e.g., phenyl) or completely saturated cycloalkyl.

[0114] The optionally substituted C_{3-8} cycloalkenyl is particularly preferably cyclohexenyl at the ring Cy.

[0115] The C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group B is that wherein the above-defined C_{6-14} aryl C_{1-6} alkyl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted arylalkyl. The substituent(s) is(are) selected from the above-mentioned group B.

[0116] Examples thereof include benzyl, 1-naphthylmethyl, 2-naphthylmethyl, phenethyl, 3-phenylpropyl, 2-phenylpropyl, 3-fluorobenzyl, 4-fluorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2,4-dichlorobenzyl, 3,5-dichlorobenzyl, pentafluorobenzyl, 4-methylbenzyl, 4-tert-butylbenzyl, 2-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-nitrobenzyl, 4-cyanobenzyl, 4-acetylbenzyl, 4-carboxylbenzyl, 4-carbamoylbenzyl, 4-aminobenzyl, 4-dimethylaminobenzyl, 4-acetylaminobenzyl, 4-(methylsulfonylamino)benzyl, 4-methoxybenzyl, 3,4,5-trimethoxybenzyl, 4-methylthiobenzyl, 4-methylsulfonylbenzyl, 4-aminosulfonylbenzyl, 3-nitro-4-methoxybenzyl and 4-nitro-3-methoxybenzyl.

[0117] The C_{6-14} aryl C_{1-6} alkyl moiety is preferably benzyl or phenethyl, particularly preferably benzyl. The group B is preferably the above-defined halogen atom, nitro, the above-defined C_{1-6} alkyl, the above-defined halogenated C_{1-6} alkyl or $-(CH_2)_r-OR^{b1}$. Examples thereof include fluorine atom, chlorine atom, nitro, methyl, tert-butyl, trifluoromethyl, methoxy or trifluoromethyloxy, particularly preferably fluorine atom or chlorine atom.

[0118] The specific C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group B at R^{a12} and R^{a13} is preferably benzyl, phenethyl, 3-chlorobenzyl, 4-chlorobenzyl, 4-tert-butylbenzyl or 3-trifluoromethylbenzyl, it is preferably benzyl at R^{a1}, R^{a19}, R^{a27}, R^{a28}, R^{a31} and R^{b5}, it is preferably benzyl, phenethyl, 4-fluorobenzyl, 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 4-tert-butylbenzyl or 4-trifluoromethylbenzyl at R^{a20}, and 4-chlorobenzyl, 3,5-dichlorobenzyl or 4-trifluoromethylbenzyl at R^{a22} and R^{a23}.

[0119] It is particularly preferably benzyl at other substituents.

[0120] The C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group D is that wherein the above-defined C_{6-14} aryl C_{1-6} alkyl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted aryl. The substituent(s) is(are) selected from the substituent(s) of the above-mentioned group D (substituents shown under (a) to (p)).

[0121] Examples of group D include fluorine atom, chlorine atom, bromine atom, nitro, cyano, methyl, ethyl, propyl, isopropyl, tert-butyl, trifluoromethyl, hydroxymethyl, 2-hydroxyethyl, methoxymethyl, 2-carboxylethyl, methoxycarbonylmethyl, ethoxycarbonylmethyl, acetyl, carboxyl, methoxycarbonyl, ethoxycarbonyl, carbamoyl, methylaminocarbonyl, isopropylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, (2-hydroxyethyl)aminocarbonyl, (carboxylmethyl)aminocarbonyl, hydroxyl group, methoxy, ethoxy, isopropyloxy, hydroxymethyloxy, carboxylmethyloxy, (dimethylaminocarbonyl)methyloxy, amino, methylamino, dimethylamino, diethylamino, acetylamino, methylsulfonylamino, methylthio, methylsulfonyl, methylsulfinyl, aminosulfonyl, methylaminosulfonyl and dimethylaminosulfonyl.

[0122] Examples of C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group D include benzyl, 1-naphthylmethyl, 2-naphthylmethyl, phenethyl, 3-phenylpropyl, 2-phenylpropyl, 3-fluorobenzyl, 4-fluorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2,4-dichlorobenzyl, 3,5-dichlorobenzyl, 4-bromobenzyl, 4-nitrobenzyl, pentafluorobenzyl, 4-methylbenzyl, 4-tert-butylbenzyl, 2-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-(hydroxymethyl)benzyl, 4- (methoxymethyl)benzyl, 4-(2-carboxylethyl)benzyl, 3-carboxylbenzyl, 4-carboxylbenzyl, 4-methoxybenzyl, 3,4,5-trimethoxybenzyl, 4-carbamoylbenzyl, 4-methylthiobenzyl, 4-(dimethylaminocarbonyl)benzyl, 4-methylsulfonylbenzyl, 4-(acetylamino)benzyl, 4-cyanobenzyl, 4-acetylbenzyl, 4-aminobenzyl, 4-dimethylaminobenzyl, 4-(methylsulfonylamino) benzyl, 4-methylsulfinylbenzyl, 4-aminosulfonylbenzyl, (3-nitro-4-methoxyphenyl)methyl and (4-nitro-3-methoxyphenyl)methyl.

[0123] At Z and Z', the C_{6-14} aryl C_{1-6} alkyl moiety is preferably benzyl or phenethyl, and the group D here is preferably the above-defined halogen atom, nitro, the above-defined optionally substituted C_{1-6} alkyl, $-(CH_2)_t-COOR^{a19}$, $-(CH_2)_t-CONR^{a27}R^{a28}$, $-(CH_2)_t-OR^{a20}$, $-(CH_2)_t-NR^{a29}CO-R^{a24}$, $-(CH_2)_t-S(O)_q-R^{a25}$ or $-(CH_2)_t-SO_2-NHR^{a26}$.

[0124] The C_{6-14} aryl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group D is preferably benzyl, 3-fluorobenzyl, 4-fluorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 3,5-dichlorobenzyl, 4-bromobenzyl, 4-nitrobenzyl, 4-methylbenzyl, 4-tert-butylbenzyl, 2-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-(hydroxymethyl)benzyl, 4-(methoxymethyl)benzyl, 4-(2-carboxylethyl)benzyl, 3-carboxylbenzyl, 4-carboxylbenzyl, 4-methoxybenzyl, 3,4,5-trimethoxybenzyl, 4-carbamoylbenzyl, 4-methylthiobenzyl, 4-(dimethylaminocarbonyl)benzyl, 4-methylsulfonylbenzyl, 4-acetylaminobenzyl, 4-methylsulfinylbenzyl or 4-aminosulfonylbenzyl.

[0125] It is particularly preferably the above-defined halogen atom, the above-defined optionally substituted C_{1-6} alkyl, $-(CH_2)_t-COOR^{a19}$, $-(CH_2)_t-CONR^{a27}R^{a28}$, $-(CH_2)_t-OR^{a20}$ or $-(CH_2)_t-S(O)_q-R^{a25}$. Examples thereof include fluorine atom, chlorine atom, bromine atom, nitro, methyl, tert-butyl, carboxyl, trifluoromethyl, hydroxymethyl, methoxymethyl, 2-carboxylethyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl and acetylamino. It is more preferably fluorine atom, chlorine atom, methyl, tert-butyl, carboxyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl or methylsulfonyl, most preferably fluorine atom or chlorine atom.

[0126] The heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group B is that wherein the above-defined heterocycle C_{1-6} alkyl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted heterocycle C_{1-6} alkyl. The substituent(s) is(are) selected from the above-mentioned group B.

[0127] Examples thereof include 2-pyridylmethyl, 3-pyridylmethyl, 2-chloropyridin-4-ylmethyl, 4-pyridylmethyl, pyrrolylmethyl, imidazolylmethyl, 2-thienylmethyl, 3-thienylmethyl, 2-furylmethyl, 2-oxazolylmethyl, 5-isothiazolylmethyl, 2-methyloxazol-4-ylmethyl, 2-thiazolylmethyl, 4-thiazolylmethyl, 5-thiazolylmethyl, 2-methylthiazol-4-ylmethyl, 2-methylthiazol-5-ylmethyl, 2,5-dimethylthiazol-4-ylmethyl, 4-methylthiazol-2-ylmethyl, 2,4-dimethylthiazol-5-ylmethyl, 2-isothiazolylmethyl, 2-pyrrolinylmethyl, pyrrolidinylmethyl, piperidylmethyl, 4-piperidylmethyl, 1-methylpiperidin-4-ylmethyl, 2-(4-hydroxypiperidino)ethyl, 1-(tert-butoxycarbonyl)piperidin-4-ylmethyl, 1-acetylpiperidin-4-ylmethyl, 1-methylsulfonylpiperidin-4-ylmethyl, piperazinylmethyl, morpholinomethyl, thiomorpholinylmethyl, 1-tetrahydropyranylmethyl, 2-quinolylmethyl, 1-isoquinolylmethyl and the like.

[0128] The heterocyclic moiety is preferably a heterocyclic group which is a 5-membered or 6-membered monocyclic group. Examples thereof include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl and tetrahydropyranyl, and the alkyl moiety thereof is preferably straight chain alkyl having 1 to 4 carbon atoms. The group B here is preferably the above-defined halogen atom, the above-defined C_{1-6} alkyl, the above-defined halogenated C_{1-6} alkyl, the above-defined C_{1-6} alkanoyl, $-(CH_2)_r-COOR^{b1}$, $-(CH_2)_r-CONR^{b1}R^{b2}$ or $-(CH_2)_r-OR^{b1}$.

[0129] Examples of heterocycle C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from group B preferably include 2-pyridylmethyl, 3-pyridylmethyl, 2-chloropyridin-4-ylmethyl, 4-pyridylmethyl, piperidin-4-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-(4-hydroxypiperidino)ethyl, 1-acetylpiperidin-4-ylmethyl, 1-(tert-butoxycarbonyl) piperidin-4-ylmethyl, 1-(methylsulfonyl)-piperidin-4-ylmethyl, 2-thiazolylmethyl, 4-thiazolylmethyl, 2-methylthiazolin-4-yl-

methyl, 2,4-dimethylthiazolin-5-ylmethyl and 4-methylthiazol-2-ylmethyl. Particularly preferably, it is 2-pyridylmethyl, 3-pyridylmethyl, 2-chloropyridin-4-ylmethyl, 4-pyridylmethyl, piperidin-4-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-(4-hydroxypiperidino)ethyl, 1-acetylpiperidin-4-ylmethyl, 1-(tert-butoxycarbonyl)piperidin-4-ylmethyl, 1-(methylsulfonyl)piperidin-4-ylmethyl, 2-methylthiazolin-4-ylmethyl, 2,4-dimethylthiazolin-5-ylmethyl or 4-methylthiazol-2-ylmethyl at R^{a20}, 2-pyridylmethyl at R^{a22} and R^{a23}, and 4-pyridylmethyl or 4-methylthiazol-2-ylmethyl at R^{a27} and R^{a28}.

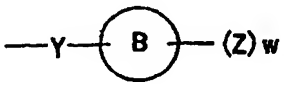
[0130] The C_{3-8} cycloalkyl C_{1-6} alkyl optionally substituted by 1 to 5 substituent(s) selected from the above group B is that wherein the above-defined C_{3-8} cycloalkyl C_{1-6} alkyl is optionally substituted by 1 to 5 substituent(s), and includes unsubstituted cycloalkylalkyl. The substituents are selected from the above group B.

[0131] Specific examples thereof include cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, 2-(cyclopentyl)ethyl, 2-(cyclohexyl)ethyl, cycloheptylmethyl, 4-fluorocyclohexylmethyl, 2-methylcyclopentylmethyl, 3-methylcyclohexylmethyl, 4-methylcyclohexylmethyl, 4,4-dimethylcyclohexylmethyl, 3,5-dimethylcyclohexylmethyl, 4-tert-butylcyclohexylmethyl, 4-hydroxycyclohexylmethyl, 4-methoxycyclohexylmethyl and 2,3,4,5,6-pentafluorocyclohexylmethyl.

[0132] Also exemplified are those wherein cyclopentylmethyl or cyclohexylmethyl is substituted by fluorine atom, chlorine atom, bromine atom, nito, methyl, tert-butyl, carboxyl, trifluoromethyl, hydroxymethyl, methoxymethyl, 2-carboxylethyl, methoxy, carbamoyl, methylthio, dimethylaminocarbonyl, methylsulfonyl or acetylamino.

[0133] At cycloalkyl moiety, it is preferably cyclopentylmethyl or cyclohexylmethyl, and at R^{a20}, R^{a27} and R^{a28}, it is particularly preferably cyclohexylmethyl.

[0134] In formula [I], X is preferably

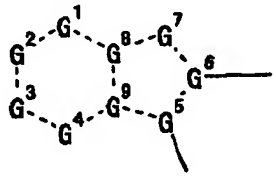


wherein each symbol is as defined above.

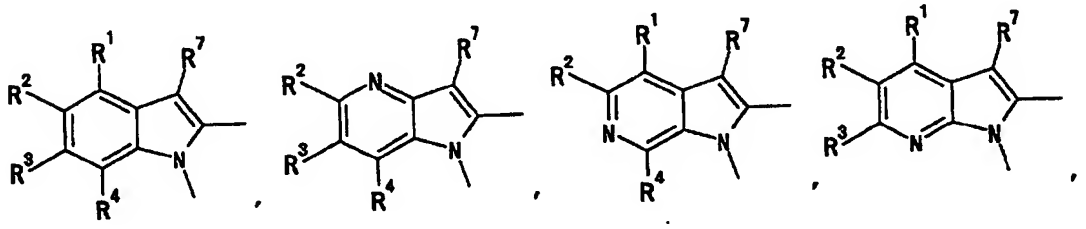
[0135] G^1, G^2, G^3 and G^4 are each preferably (C-R^1), (C-R^2), (C-R^3) and (C-R^4), G^5 is preferably a nitrogen atom, and G^6, G^8 and G^9 are preferably a carbon atom. G^7 is preferably C(-R^7) or unsubstituted nitrogen atom, wherein R^7 is preferably hydrogen atom.

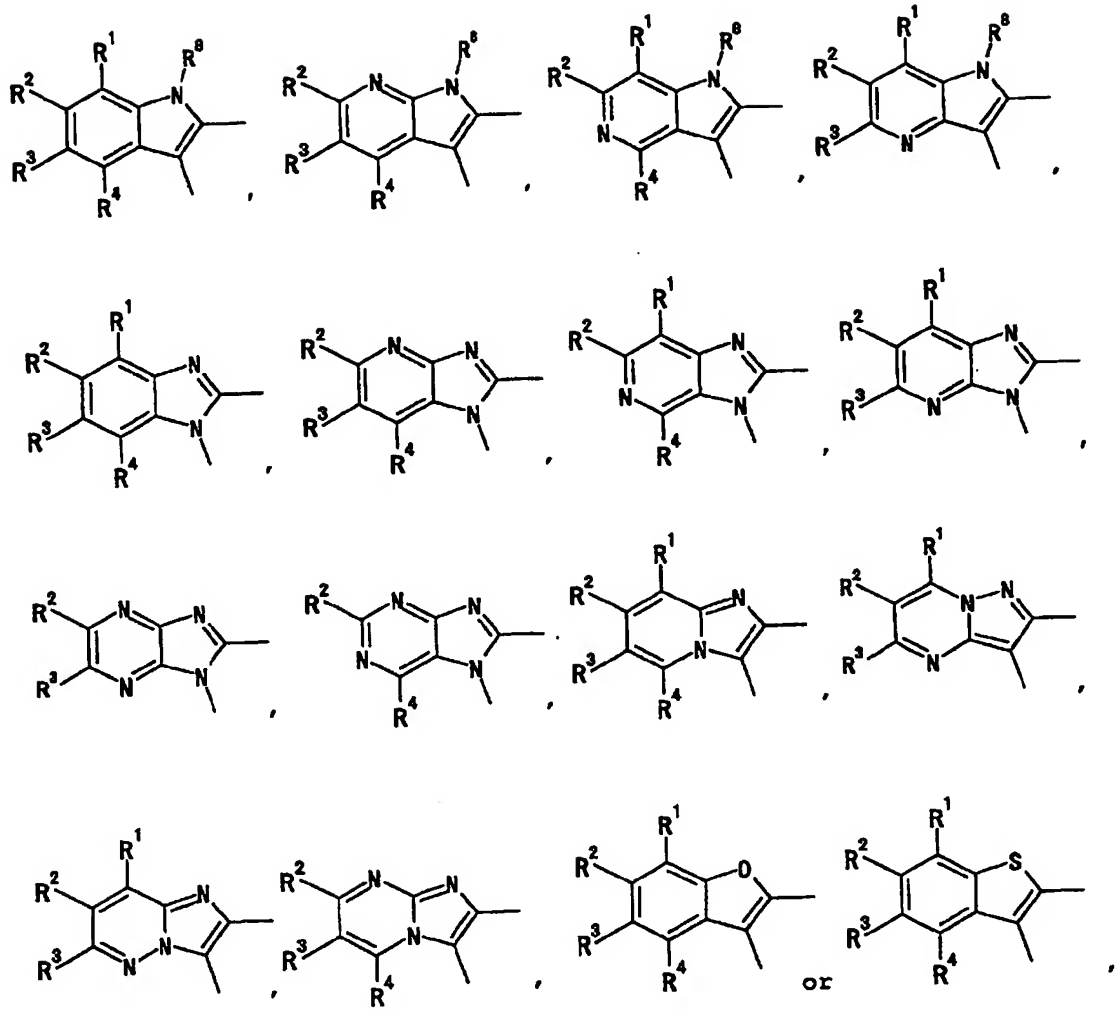
[0136] A preferable combination is G^2 of (C-R^2) and G^6 of a carbon atom, particularly preferably G^2 of (C-R^2), G^6 of a carbon atom and G^5 of a nitrogen atom, most preferably G^2 of (C-R^2), G^6 of a carbon atom, G^5 of a nitrogen atom and G^7 of unsubstituted nitrogen atom.

[0137] In formulas [I] and [Ii], 1 to 4 of G^1 to G^9 in the moiety

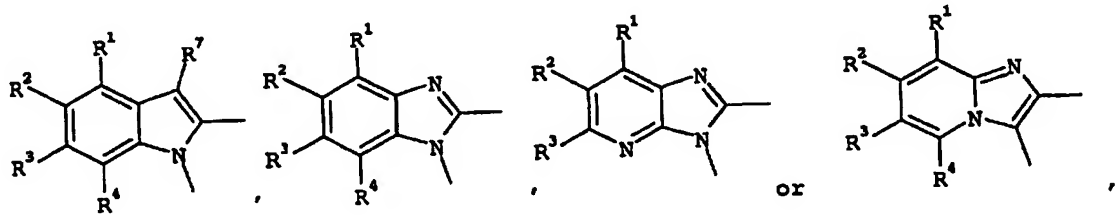


is(are) preferably a nitrogen atom, specifically preferably

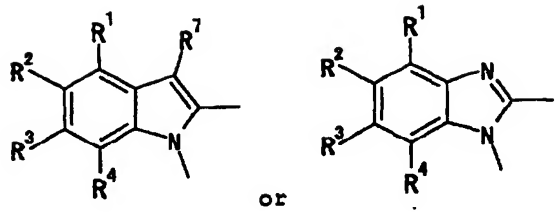




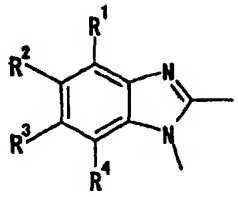
particularly preferably



more preferably



most preferably



[0138] R^1 and R^4 are preferably hydrogen atom. R^2 is preferably carboxyl, $-COOR^{a1}$, $-CONR^{a2}R^{a3}$ or $-SO_2R^{a7}$ (each symbol is as defined above), particularly preferably carboxyl, $-COOR^{a1}$ or $-SO_2R^{a7}$, more preferably carboxyl or $-COOR^{a1}$, most preferably carboxyl. R^3 is preferably hydrogen atom or $-OR^{a6}$ (R^{a6} is as defined above), particularly preferably hydrogen atom.

[0139] The ring Cy and ring Cy' are preferably cyclopentyl, cyclohexyl, cycloheptyl or tetrahydrothiopyranyl, particularly preferably cyclopentyl, cyclohexyl or cycloheptyl, more preferably cyclohexyl.

[0140] The ring A and ring A' are preferably phenyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, cyclohexyl, cyclohexenyl, furyl or thienyl, particularly preferably phenyl, pyridyl, pyrazinyl, pyrimidinyl or pyridazinyl, more preferably phenyl or pyridyl, and most preferably phenyl.

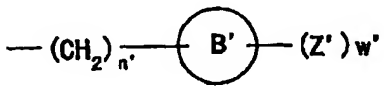
[0141] The ring B and ring B' are preferably C_{1-6} aryl or heterocyclic group, specifically preferably, phenyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,3,5-triazinyl, pyrrolyl, pyrazolyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, thienyl, furyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl or thiadiazolyl, particularly preferably phenyl, pyridyl, pyrimidinyl, 1,3,5-triazinyl or thiazolyl, more preferably, phenyl, pyridyl or thiazolyl, and most preferably phenyl or thiazolyl.

[0142] With regard to R^5 and R^6, one of them is preferably hydrogen atom and the other is halogen atom, particularly fluorine atom. Alternatively, the both arepreferably hydrogen atoms. When ring A is phenyl, R^5 and R^6 preferably are present at an ortho position from G^6. The same applies to $R^{5'}$ and $R^{6'}$.

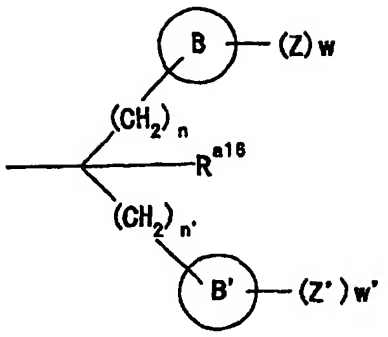
[0143] Y is preferably $-(CH_2)_m-O-(CH_2)_n-$, $-NHCO_2-$, $-CONH-CHR^{a14}-$, $-(CH_2)_m-NR^{a12}-(CH_2)_n-$, $-CONR^{a13}-(CH_2)_n-$, $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$ or $-(CH_2)_n-NR^{a12}-CHR^{a15}-$ (each symbol is as defined above), more preferably, $-(CH_2)_m-O-(CH_2)_n-$ or $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$, most preferably $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$.

[0144] The l, m and n are preferably 0 or an integer of 1 to 4, particularly preferably 0, 1 or 2, at Y. In $-(CH_2)_m-O-(CH_2)_n-$, m=n=0 or m=0 and n=1 is more preferable, most preferably m=n=0. In $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$, m=n=0, m=0 and n=1, m=1 and n=0 or m=1 and n=1 is more preferable, most preferably m=n=0.

[0145] When Y is $-O-(CH_2)_m-CR^{a15}R^{a16}-(CH_2)_n-$, R^{a16} is preferably hydrogen atom, R^{a15} is preferably



wherein the



moiety is preferably symmetric. The preferable mode of n, ring B, Z and w and the preferable mode of n', ring B', Z' and w' are the same.

[0146] When ring A is phenyl, X or Y is preferably present at the para-position relative to G^6. When ring B and ring B' are phenyl, Z is preferably present at the ortho or meta-position relative to Y. It is preferable that the 3-position on phenyl have one substituent or the 2-position and the 5-position on phenyl each have one substituent.

[0147] When ring B is thiazolyl, Y is preferably substituted at the 5-position, and Z is preferably substituted at the 2-position, the 4-position or the 2-position and the 4-position. Similarly, when ring B' is thiazolyl, $(CH_2)_{n'}$ is also preferably substituted at the 5-position, and Z' is preferably substituted at the 2-position, the 4-position or the 2-position and the 4-position.

[0148] Z and Z' are preferably group D, "C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D" or "heterocyclic group optionally substituted by 1 to 5 substituent(s) selected from group D", particularly preferably group D or "C_{6-14} aryl optionally substituted by 1 to 5 substituent(s) selected from group D".

[0149] More preferably, they are the above-defined halogen atom, nitro, the above-defined optionally substituted C_{1-6} alkyl, $-(CH_2)_t-COOR^{a19}$-$(CH_2)_t-CONR^{a27}R^{a28}$, $-(CH_2)_t-OR^{a20}$, $(CH_2)_t-NR^{a29}CO-R^{a24}$, $-(CH_2)_t-S(O)_q-R^{a25}$ or $-(CH_2)_t-SO_2-NHR^{a26}$, or C_{6-14} aryl or heterocyclic group optionally substituted by these.

With regard to Z and Z', the preferable mode of group D that directly substitutes each ring B and ring B' and the preferable mode of group D that substitutes C_{6-14} aryl, C_{3-8} cycloalkyl, C_{6-14} aryl C_{1-6} alkyl or heterocyclic group are the same, wherein they may be the same with or different from each other.

[0150] Specific examples of the substituent preferably include fluorine atom, chlorine atom, bromine atom, nitro, cyano, methyl, ethyl, propyl, isopropyl, tert-butyl, trifluoromethyl, hydroxymethyl, 2-hydroxyethyl, methoxymethyl, 2-carboxylethyl, methoxycarbonylmethyl, ethoxycarbonylmethyl, acetyl, carboxyl, methoxycarbonyl, ethoxycarbonyl, carbamoyl, methylaminocarbonyl, isopropylaminocarbonyl, dimethylaminocarbonyl, diethylamino-carbonyl, (2-hydroxyethyl)aminocarbonyl, (carboxylmethyl)-aminocarbonyl, hydroxyl group, methoxy, ethoxy, propyloxy, isopropyloxy, butyloxy, isopentyloxy, 2-isopentenyloxy, 3-isohexenyloxy, 4-methyl-3-pentenyloxy, 2-propynyloxy, trifluoromethyloxy, hydroxymethyloxy, carboxylmethyloxy, (dimethylaminocarbonyl)methyloxy, amino, methylamino, dimethylamino, diethylamino, acetylamino, methylsulfonylamino, methylthio, methylsulfonyl, methylsulfinyl, aminosulfonyl, methylaminosulfonyl, dimethylaminosulfonyl, tert-butylaminosulfonyl, phenyl, 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,5-dichlorophenyl, 4-bromophenyl, 4-nitrophenyl, 4-cyanophenyl, 4-methylphenyl, 4-ethylphenyl, 4-propylphenyl, 4-isopropylphenyl, 4-tert-butylphenyl, 2-trifluoromethylphenyl, 4-trifluoromethylphenyl, 4-(hydroxymethyl) phenyl, 4-(2-hydroxyethyl)phenyl, 4-(methoxymethyl)phenyl, 4- (2-carboxylethyl)phenyl, 4-(methoxycarbonylmethyl) phenyl, 4-(ethoxycarbonylmethyl)phenyl, 4-acetylphenyl, 3-carboxylphenyl, 4-carboxylphenyl, 4-(methoxycarbonyl) phenyl, 4-(ethoxycarbonyl)-phenyl, 4-carbamoylphenyl, 4-(methylaminocarbonyl)phenyl, 4-(isopropylaminocarbonyl) phenyl, 4-(dimethylaminocarbonyl)phenyl, 4-(diethylaminocarbonyl)phenyl, 4-[(2-hydroxyethyl)-aminocarbonyl]phenyl, 4-[(carboxylmethyl)aminocarbonyl]phenyl, 4-hydroxyphenyl, 4-methoxyphenyl, 3,4,5-trimethoxyphenyl, 4-ethoxyphenyl, 4-propyloxyphenyl, 4-isopropyloxyphenyl, 4-butyloxyphenyl, 4-isopentyloxyphenyl, 4-(2-isopentenyloxy)phenyl, 4-(3-isohexenyloxy)phenyl, 4-(4-methyl-3-pentenyloxy)phenyl, 4-(2-propynyloxy)phenyl, 4-(trifluoromethyloxy) phenyl, 4-(hydroxymethyloxy)phenyl, 4-(carboxylmethyloxy)phenyl, 4-[(dimethylaminocarbonyl)methyloxy]phenyl, 4-aminophenyl, 4-(methylamino)phenyl, 4-(dimethylaminophenyl), 4-(diethylamino)-phenyl, 4-(acetylamino)phenyl, 4-(methylsulfonylamino)phenyl, 4-(methylthio)phenyl, 4- (methylsulfonyl)phenyl, 4- (methylsulfinyl)-phenyl, 4- (aminosulfonyl)phenyl, 4-(methylaminosulfonyl) phenyl, 4-(dimethylaminosulfonyl)phenyl, 4-(tert-butylaminosulfonyl)phenyl, cyclohexyl, benzyl, 4-chlorobenzyl, phenethyl, benzyloxy, 4-fluorobenzyloxy, 2-chlorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-tert-butylbenzyloxy, 4-trifluoromethylbenzyloxy, phenethyloxy, 2-thienyl, 2-thiazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidinyl, 5-tetrazolyl, piperidino, piperidinocarbonyl, 4-hydroxypiperidinocarbonyl, 1-piperazinylcarbonyl, 1-pyrrolidinylcarbonyl, morpholinocarbonyl, 4-thiomorpholinylcarbonyl, phenoxy, 2,4-dichlorophenoxy, tet-

rahydropyranyloxy, 2-pyridylmethyloxy, 3-pyridylmethyloxy, 2-chloropyridin-4-ylmethyloxy, 4-pyridylmethyloxy, 2-piperidylmethyloxy, 3-piperidylmethyloxy, 4-piperidylmethyloxy, 1-methylpiperidin-4-ylmethyloxy, 1-acetylpiperidin-4-ylmethyloxy, 1-(tert-butoxycarbonyl)piperidin-4-ylmethyloxy, 1-(methylsulfonyl)-piperidin-4-ylmethyloxy, 2-methylthiazolin-4-yloxy, 2,4-dimethylthiazolin-5-yloxy, dimethylaminocarbonylmethyloxy, piperidinocarbonylmethyloxy, 2-methylthiazol-4-yl, (2-methylthiazol-4-yl) methyloxy, (2,4-dimethylthiazol-5-yl)methyloxy, benzoyl, 3-fluorobenzoyl, 4-chlorobenzylamino, 3,5-dichlorobenzylamino, 4-trifluoromethylbenzylamino, 2-pyridylmethylamino, benzoylamino, 4-chlorobenzoylamino, 4-trifluoromethylbenzoylamino, 3,5-dichlorobenzoylamino, 3-nitro-4-methoxybenzoylamino, 4-nitro-3-methoxybenzoylamino, 3-pyridylcarbonylamino, 4-methylphenylsulfonylamino, 2-thiazolylaminosulfonyl, 2-pyridylaminosulfonyl, benzylaminocarbonyl, N-benzyl-N-methylaminocarbonyl, (4-pyridylmethyl)-aminocarbonyl or (cyclohexylmethyl)aminocarbonyl, 2-hydroxyethyloxy, 3-hydroxypropyloxy, 3-hydroxypyrrolidinylcarbonyl, 3-hydroxypiperidinocarbonyl, 3,4-dihydroxypiperidinocarbonyl, 4-methoxypiperidinocarbonyl, 4-carboxypiperidinocarbonyl, 4-(hydroxymethyl)piperidinocarbonyl, 2-oxopiperidinocarbonyl, 4-oxopiperidinocarbonyl, 2,2,6,6-tetramethylpiperidinocarbonyl, 2,2,6,6-tetramethyl-4-hydroxypiperidinocarbonyl, 1-oxothiomorpholin-4-ylcarbonyl, 1,1-dioxothiomorpholin-4-ylcarbonyl, 1-(methylsulfonyl)piperidin-4-ylaminocarbonyl, 4-methylsulfonylpiperazinylcarbonyl, N,N-bis(2-hydroxyethyl)-aminocarbonyl, phenylaminocarbonyl, cyclohexylaminocarbonyl, 4-hydroxycyclohexylaminocarbonyl, 4-methylthiazol-2-ylmethylaminocarbonyl, 2-(4-hydroxypiperidino)ethyloxy, 2-pyridylmethylaminocarbonyl, 3-pyridylmethylaminocarbonyl, N-methyl-N-(4-pyridylmethyl)aminocarbonyl, cyclohexylmethyloxy, 4-hydroxypiperidinocarbonylmethyloxy and 4-methylthiazol-2-ylmethyloxy.

[0151] Particularly preferable examples of the substituent include fluorine atom, chlorine atom, bromine atom, nitro, cyano, methyl, hydroxymethyl, carboxyl, carbamoyl, methylaminocarbonyl, isopropylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, (2-hydroxylethyl)aminocarbonyl, (carboxymethyl)-aminocarbonyl, methoxy, 2-isopentenyloxy, 2-propynyloxy, methylthio, methylamino, dimethylamino, acetylamino, methylsulfonylamino, methylsulfonyl, aminosulfonyl, dimethylaminosulfonyl, tert-butylaminosulfonyl, phenyl, 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,5-dichlorophenyl, 4-nitrophenyl, 4-methylphenyl, 4-tert-butylphenyl, 4-trifluoromethylphenyl, 4-(methoxymethyl)phenyl, 4-(2-hydroxylethyl)phenyl, 3-carboxylphenyl, 4-carboxylphenyl, 4-methoxyphenyl, 4-carbamoylphenyl, 4-methylthiophenyl, 4-(dimethylaminocarbonyl)phenyl, 4-methylsulfonylphenyl, benzyl, phenethyl, benzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 2-thiazolyl, 3-pyridyl, 4-pyridyl, 4-pyridylmethyloxy, 2-piperidylmethyloxy, 3-piperidylmethyloxy, 4-piperidylmethyloxy, 1-methylpiperidin-4-ylmethyloxy, 1-acetylpiperidin-4-ylmethyloxy, 2-chloropiperidin-4-ylmethyloxy, 1-(methylsulfonyl)piperidin-4-ylmethyloxy, 2-methylthiazol-4-yl, (2-methylthiazol-4-yl)methyloxy, (2,4-dimethylthiazol-5-yl)methyloxy, 5-tetrazolyl, 3-fluorobenzoyl, piperidinocarbonyl, 4-hydroxylpiperidinocarbonyl, 1-pyrrolidinylcarbonyl, morpholinocarbonyl, 4-thiomorpholinylcarbonyl, benzylaminocarbonyl, N-benzyl-N-methylaminocarbonyl, (4-pyridylmethyl)aminocarbonyl and (cyclohexylmethyl)aminocarbonyl.

[0152] Most preferable substituents are fluorine atom, chlorine atom, methyl, hydroxymethyl, carboxyl, carbamoyl, methylaminocarbonyl, dimethylaminocarbonyl, methoxy, methylamino, acetylamino, aminosulfonyl, dimethylaminosulfonyl, tert-butylaminosulfonyl, phenyl, 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,5-dichlorophenyl, 4-methylphenyl, 4-tert-butylphenyl, 4-trifluoromethylphenyl, 4-carboxylphenyl, 4-methoxyphenyl, 4-carbamoylphenyl, 4-methylthiophenyl, 4-(dimethylaminocarbonyl)phenyl and 4-methylsulfonylphenyl.

[0153] The w is preferably 1 or 2, r and t are preferably 0, 1 or 2, particularly preferably 0 or 1, more preferably 0, p is preferably 1, and q is preferably 0 or 2.

[0154] The pharmaceutically acceptable salt may be any as long as it forms a non-toxic salt with a compound of the above-mentioned formula [I] or [II]. Such salt can be obtained by reacting the compound with an inorganic acid, such as hydrochloric acid, sulfuric acid, phosphoric acid, hydrobromic acid and the like, or an organic acid, such as oxalic acid, malonic acid, citric acid, fumaric acid, lactic acid, malic acid, succinic acid, tartaric acid, acetic acid, trifluoroacetic acid, gluconic acid, ascorbic acid, methylsulfonic acid, benzylsulfonic acid and the like, or an inorganic base, such as sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, ammonium hydroxide and the like, or an organic base, such as methylamine, diethylamine, triethylamine, triethanolamine, ethylenediamine, tris(hydroxymethyl)methylamine, guanidine, choline, cinchonine and the like, with an amino acid, such as lysine, arginine, alanine and the like. The present invention encompasses water-retaining product, hydrate and solvate of each compound.

[0155] The compounds of the above-mentioned formula [I] or [II] have various isomers. For example, E compound and Z compound are present as geometric isomers, and when the compound has an asymmetric carbon, an enantiomer and a diastereomer are present due to the asymmetric carbon. A tautomer may be also present. The present invention encompasses all of these isomers and mixtures thereof.

[0156] The present invention also encompasses prodrug and metabolite of each compound.

[0157] A prodrug means a derivative of the compound of the present invention, which is capable of chemical or metabolic decomposition, which shows inherent efficacy by reverting to the original compound after administration to a body, and which includes salts and complexes without a covalent bond.

[0158] When the inventive compound is used as a pharmaceutical preparation, the inventive compound is generally

admixed with pharmaceutically acceptable carriers, excipients, diluents, binders, disintegrators, stabilizers, preservatives, buffers, emulsifiers, aromatics, coloring agents, sweeteners, thickeners, correctives, solubilizers, and other additives such as water, vegetable oil, alcohol such as ethanol, benzyl alcohol and the like, polyethylene glycol, glycerol triacetate, gelatin, lactose, carbohydrate such as starch and the like, magnesium stearate, talc, lanolin, petrolatum and the like, and prepared into a dosage form of tablets, pills, powders, granules, suppositories, injections, eye drops, liquids, capsules, troches, aerosols, elixirs, suspensions, emulsions, syrups and the like, which can be administered systemically or topically and orally or parenterally.

[0159] While the dose varies depending on the age, body weight, general condition, treatment effect, administration route and the like, it is from 0.1 mg to 1 g for an adult per dose, which is given one to several times a day.

[0160] The prophylaxis of hepatitis C means, for example, administration of a pharmaceutical agent to an individual found to carry an HCV by a test and the like but without a symptom of hepatitis C, or to an individual who shows an improved disease state of hepatitis after a treatment of hepatitis C, but who still carries an HCV and is associated with a risk of recurrence of hepatitis.

[0161] Examples of the production method of the compound to be used for the practice of the present invention are given in the following. However, the production method of the compound of the present invention is not limited to these examples.

[0162] Even if no directly corresponding disclosure is found in the following Production Methods, the steps may be modified for efficient production of the compound, such as introduction of a protecting group into a functional group with deprotection in a subsequent step, and changing the order of Production Methods and steps.

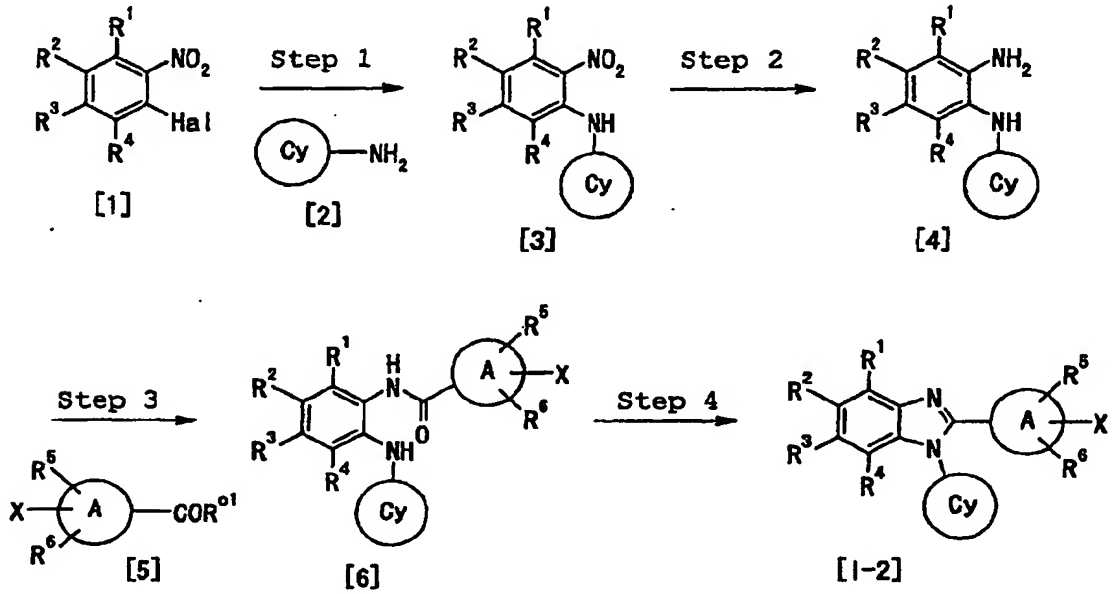
[0163] The treatment after reaction in each step may be conventional ones, for which typical methods, such as isolation and purification, crystallization, recrystallization, silica gel chromatography, preparative HPLC and the like, can be appropriately selected and combined.

Production Method 1

[0164] In this Production Method, a benzimidazole compound is formed from a nitrobenzene compound.

Production Method 1-1

[0165]



wherein Hal is halogen atom, such as chlorine atom, bromine atom and the like, R^{c1} is halogen atom, such as chlorine atom, bromine atom and the like, or hydroxyl group, and other symbols are as defined above.

Step 1

[0166] A compound [1] obtained by a conventional method or a commercially available compound [1] is reacted with amine compound [2] in a solvent such as N,N-dimethylformamide (DMF), acetonitrile, tetrahydrofuran (THF), toluene and the like in the presence or absence of a base such as potassium carbonate, triethylamine, potassium t-butoxide and the like at room temperature or with heating to give compound [3].

Step 2

[0167] The compound [3] is hydrogenated in a solvent such as methanol, ethanol, THF, ethyl acetate, acetic acid, water and the like in the presence of a catalyst such as palladium carbon, palladium hydroxide, platinum oxide, Raney nickel and the like at room temperature or with heating to give compound [4]. In addition, compound [3] is reduced with a reducing agent such as zinc, iron, tin(II) chloride, sodium sulfite and the like, or reacted with hydrazine in the presence of iron(III) chloride to give compound [4].

Step 3

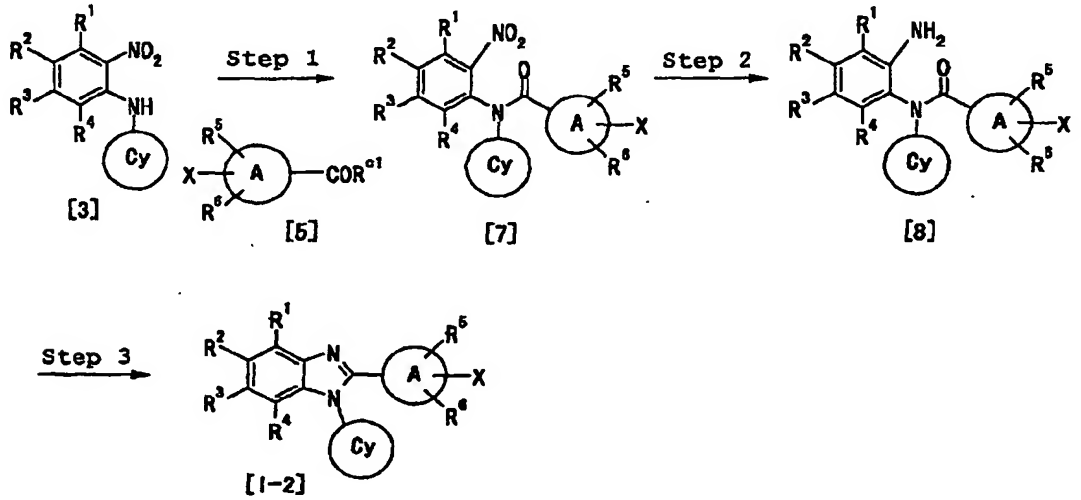
[0168] The compound [4] is condensed with carboxylic acid compound [5] in a solvent such as DMF, acetonitrile, THF, chloroform, ethyl acetate, methylene chloride, toluene and the like using a condensing agent such as dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, diphenylphosphoryl azide and the like and, where necessary, adding N-hydroxysuccinimide, 1-hydroxybenzotriazole and the like to give amide compound [6]. Alternatively, amide compound [6] can be obtained from compound [5] as follows. The carboxylic acid compound [5] is converted to an acid halide derived with thionyl chloride, oxalyl chloride and the like, or an active ester (e.g., mixed acid anhydride derived with ethyl chlorocarbonate and the like), which is then reacted in the presence of a base, such as triethylamine, potassium carbonate, pyridine and the like, or in an amine solvent, such as pyridine and the like, to give amide compound [6].

Step 4

[0169] The compound [6] is heated in a solvent such as ethanol, methanol, toluene, DMF, chloroform and the like or without a solvent in the presence of an acid such as acetic acid, formic acid, hydrochloric acid, dilute sulfuric acid, phosphoric acid, polyphosphoric acid, p-toluenesulfonic acid and the like, a halogenating agent such as zinc chloride, phosphorus oxychloride, thionyl chloride and the like or acid anhydride such as acetic anhydride and the like, to allow cyclization to give compound [I-2].

Production Method 1-2

[0170] This Production Method is an alternative method for producing compound [I-2].



wherein each symbol is as defined above.

Step 1

[0171] The compound [3] obtained in the same manner as in Step 1 of Production Method 1-1 is subjected to amide condensation with compound [5] in the same manner as in Step 3 of Production Method 1-1 to give compound [7].

Step 2

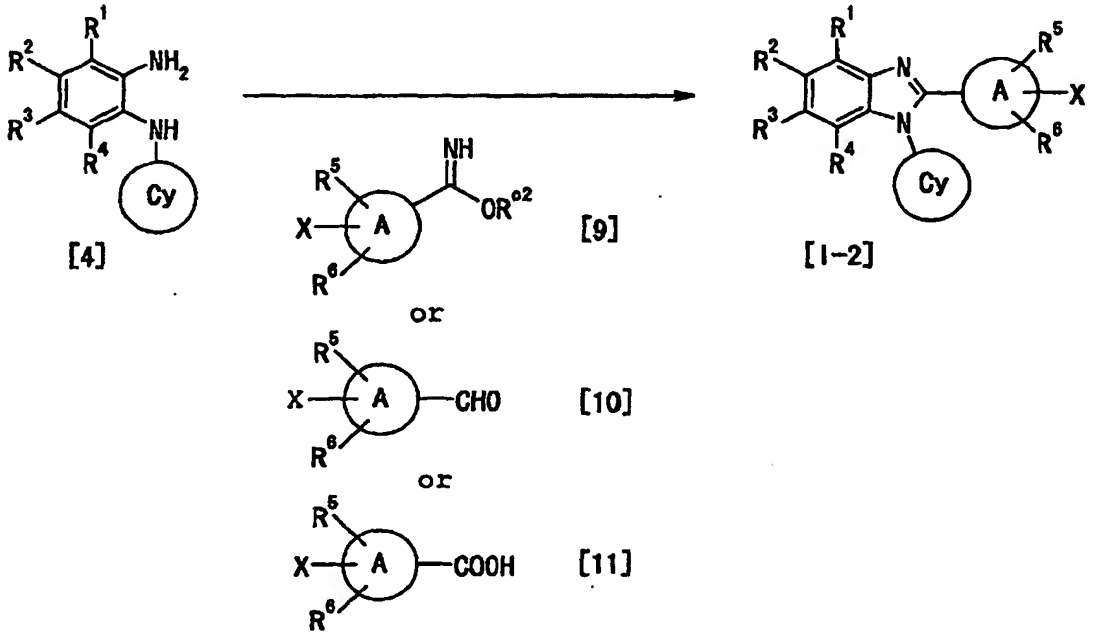
[0172] The compound [7] is reduced in the same manner as in Step 2 of Production Method 1-1 to give compound [8].

Step 3

[0173] The compound [8] is subjected to cyclization in the same manner as in Step 4 of Production Method 1-1 to give compound [I-2].

Production Method 1-3

[0174]



wherein R^{c2} is alkyl such as methyl, ethyl and the like, and other symbols are as defined above.

[0175] The compound [4] is reacted with imidate compound [9] in a solvent such as methanol, ethanol, acetic acid, DMF, THF, chloroform and the like at room temperature or with heating to give compound [I-2].

[0176] In addition, compound [4] may be reacted with aldehyde compound [10] in a solvent such as acetic acid, formic acid, acetonitrile, DMF, nitrobenzene, toluene and the like in the presence or absence of an oxidizing agent such as benzofuroxan, manganese dioxide, 2,3-dichloro-5,6-dicyano-p-benzbquinone, iodine, potassium ferricyanide and the like with heating to give compound [I-2].

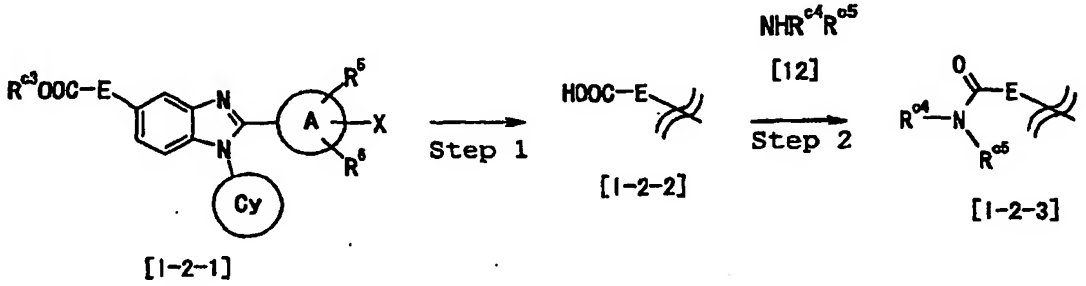
[0177] Alternatively, compound [4] and carboxylic acid compound [11] may be heated to allow reaction in the presence of polyphosphoric acid, phosphoric acid, phosphorus oxychloride, hydrochloric acid and the like to give compound [I-2].

Production Method 2

[0178] In this Production Method, conversion of the substituents (R^1, R^2, R^3, R^4) on the benzene ring of benzimidazole is shown. While a method of converting R^2 when R^1, R^3 and R^4 are hydrogen atoms is shown, this Production Method is applicable irrespective of the position of substitution.

Production Method 2-1

[0179] Conversion of carboxylic acid ester moiety to amide



[I-2-1] [I-2-2] [I-2-3]

wherein E is a single bond, $-(CH_2)_s-$, $-O-(CH_2)_s-$ or $-NH-(CH_2)_s-$(wherein s is an integer of 1 to 6), R^{c3}, R^{c4} and R^{c5} are C_{1-6} alkyl, and other symbols are as defined above.

Step 1

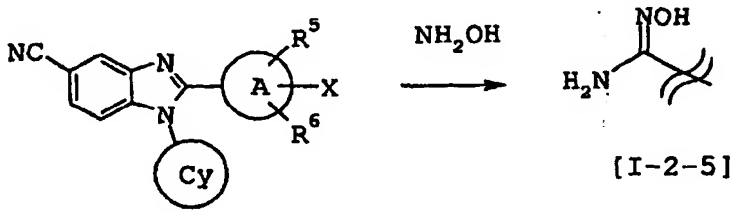
[0180] The compound [I-2-1] obtained in the same manner as in the above-mentioned Production Method is subjected to hydrolysis in a solvent such as methanol, ethanol, THF, dioxane and the like, or in a mixed solvent of these solvents and water under basic conditions with sodium hydroxide, potassium hydroxide, potassium carbonate, lithium hydroxide and the like or under acidic conditions with hydrochloric acid, sulfuric acid and the like to give compound [I-2-2].

Step 2

[0181] The compound [I-2-2] is reacted with compound [12] in the same manner as in Step 3 of Production Method 1-1 to give compound [I-2-3].

Production Method 2-2

[0182] Conversion of cyano group to substituted amidino group



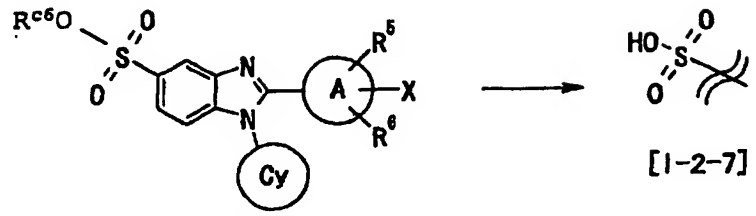
[I-2-4] [I-2-5]

wherein each symbol is as defined above.

[0183] The compound [1-2-4] obtained in the same manner as in the above-mentioned Production Method is reacted with hydroxylamine in a solvent such as water, methanol, ethanol, THF, DMF and the like to give compound [I-2-5]. When a salt of hydroxylamine such as hydrochloride and the like is used, the reaction is carried out in the presence of a base such as sodium hydrogencarbonate, sodium hydroxide, triethylamine and the like.

Production Method 2-3

[0184] Conversion of sulfonic acid ester moiety to sulfonic acid



[I-2-6] [I-2-7]

wherein R^{c6} is C_{1-6} alkyl, and other symbols are as defined above.

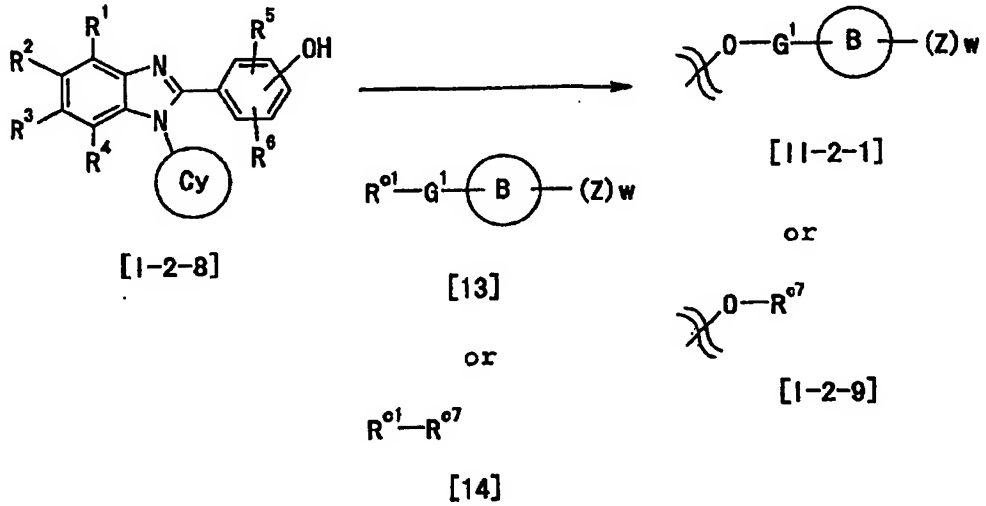
[0185] The compound [I-2-6] obtained in the same manner as in the above-mentioned Production Method is reacted with iodide salt such as sodium iodide, lithium iodide and the like, bromide salt such as sodium bromide, trimethylammonium bromide and the like, amine such as pyridine, trimethylamine, triazole and the like, phosphine such as triphenylphosphine and the like in a solvent such as DMF, dimethyl sulfoxide (DMSO), acetonitrile, methanol, ethanol, water and the like with heating to give compound [I-2-7].

Production Method 3

[0186] This Production Method relates to convertion of the substituent(s) on phenyl group at the 2-position of benzimidazole. This Production Method can be used even when phenyl is a different ring.

Production Method 3-1

[0187] Conversion of hydroxyl group to ether



[I-2-8] [13] [II-2-1] [I-2-9] [14]

wherein R^{c7} is optionally substituted alkyl corresponding to R^{a11}, G^1 is a single bond, *-$(CH_2)_n$-, *-$(CH_2)_n$-O-, *-$(CH_2)_n$-CO- or *-$(CH_2)_m$-$CR^{a15}R^{a16}$)-$(CH_2)_n$-, wherein * show the side to be bonded to R^{c1}, and other symbols are as defined above.

[0188] When R^{c1} of compound [13] is halogen atom, compound [I-2-8] obtained in the same manner as in the above-mentioned Production Method is reacted with compound [13] in a solvent such as DMF, DMSO, acetonitrile, ethanol, THF and the like in the presence of a base such as sodium hydride, sodium hydroxide, potassium hydroxide, potassium

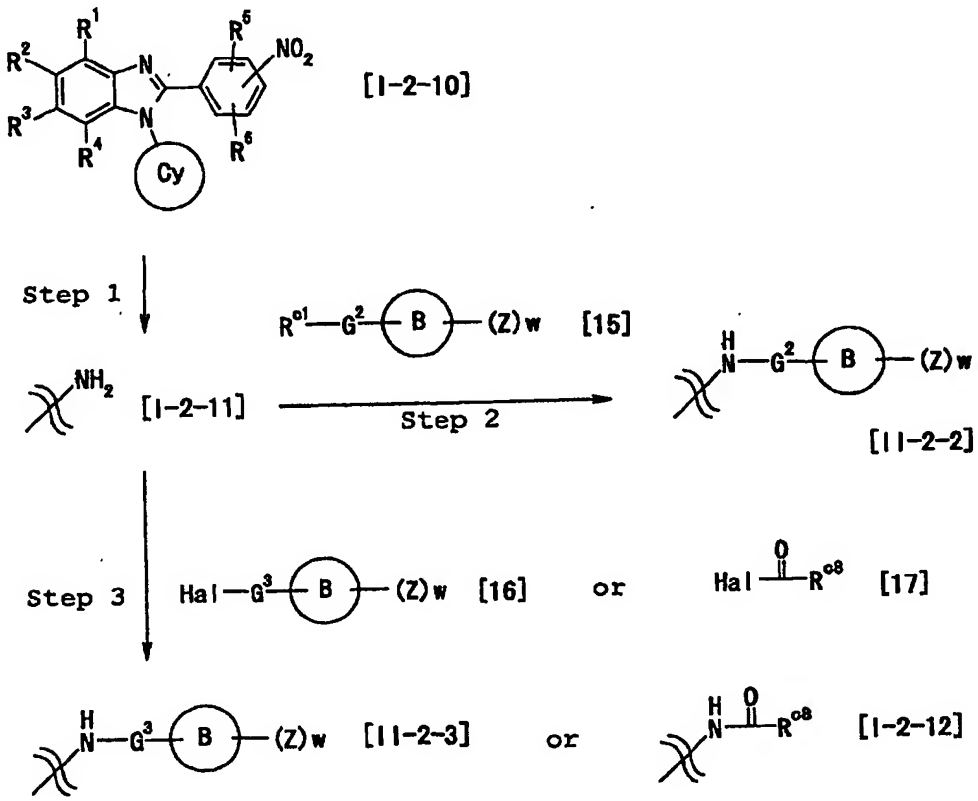
carbonate, sodium ethoxide, potassium t-butoxide and the like at room temperature or with heating to give compound [II-2-1].

[0189] When R^{c1} of compound [13] is hydroxyl group, the hydroxyl group of compound [13] is converted to halogen atom with thionyl chloride, phosphorus tribromide, carbon tetrabromide-triphenylphosphine and the like and reacted with compound [I-2-8] by the aforementioned method to give compound [II-2-1]. In this case, compound [I-2-8] may be subjected to Mitsunobu reaction with compound [13] in a solvent such as DMF, acetonitrile, THF and the like using triphenylphosphine - diethyl azodicarboxylate and the like to give compound [II-2-1].

[0190] The compound [I-2-9] can be obtained in the same manner from compound [I-2-8] and compound [14].

Production Method 3-2

[0191] Conversion of nitro to substituted amino group



wherein R^{c8} is C_{1-6} alkyl, G^2 is *-$(CH_2)_n$- or *-CHR^{a15}, G^3 is -CO-, *-CO_2-, *-CONH- or -SO_2-, and other symbols are as defined above.

Step 1

[0192] The nitro compound [I-2-10] obtained in the same manner as in the above-mentioned Production Method is reacted in the same manner as in Step 2 of Production Method 1-1 to give compound [I-2-11].

Step 2

[0193] The compound [I-2-11] is alkylated with compound [15] in the same manner as in Production Method 3-1 to give compound [II-2-2].

Step 3

[0194] When G^3 of compound [16] is -CO-, $-CO_2-$ or -CONH-, compound [I-2-11] is acylated with compound [16] in the same manner as in Step 3 of Production Method 1-1 to give compound [II-2-3].

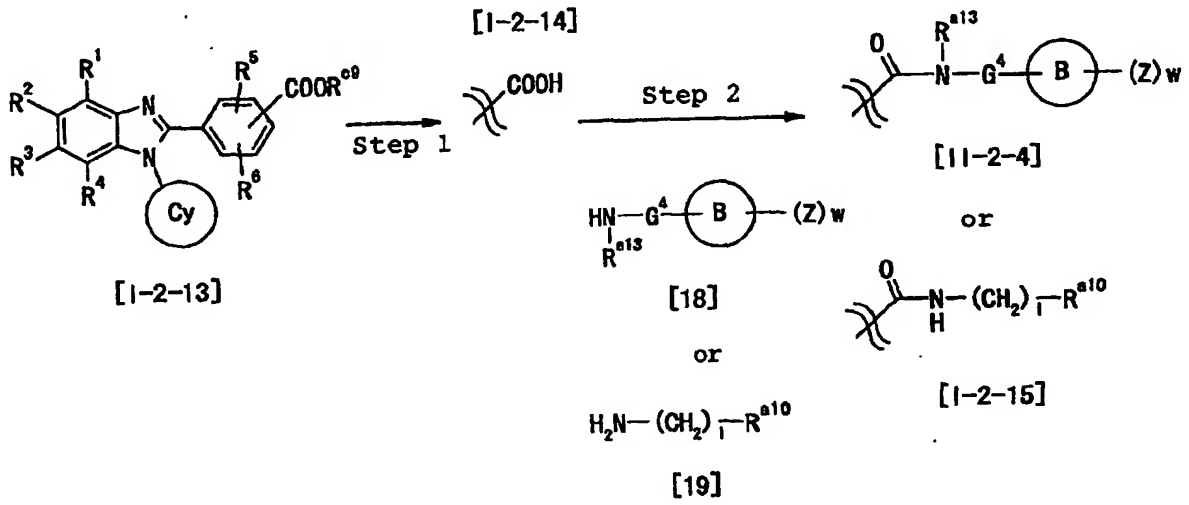
[0195] When G^3 of compound [16] is $-SO_2-$, sulfonylation is conducted using sulfonyl halide instead of acid halide used in Step 3 of Production Method 1-1 to give compound [II-2-3].

[0196] The compound [I-2-11] is acylated with compound [17] in the same manner as above to give compound [I-2-12].

[0197] This Production Method is applied in the same manner as above to give disubstituted compounds (tertiary amine) of compound [II-2-2], compound [II-2-3] and compound [I-2-12].

Production Method 3-3

[0198] Conversion of carboxylic acid ester moiety to amide



wherein R^{c9} is C_{1-6} alkyl, G^4 is #-$(CH_2)_n$-, #-$(CH_2)_n$-NH- or #-CHR^{a14}-wherein # shows the side that is bounded to amine and other symbols are as defined above.

Step 1

[0199] The compound [I-2-13] obtained in the same manner as in the above-mentioned Production Method is reacted in the same manner as in Step 1 of Production Method 2-1 to give compound [I-2-14].

Step 2

[0200] The compound [I-2-14] is reacted with compound [18] in the same manner as in Step 2 of Production Method 2-1 to give compound [II-2-4].

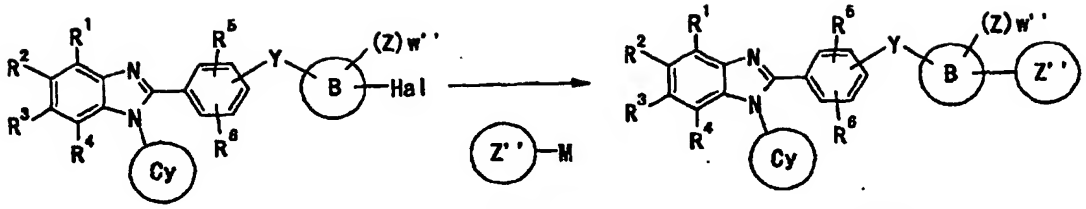
[0201] The compound [I-2-15] is obtained from compound [I-2-14] and compound [19] in the same manner as above.

Production Method 4

[0202] In this Production Method, additional substituent(s) is(are) introduced into ring B on phenyl group that substitutes the 2-position of benzimidazole. This Production Method is applicable even when phenyl is a different ring.

Production Method 4-1

[0203] Direct bonding of ring Z" to ring B



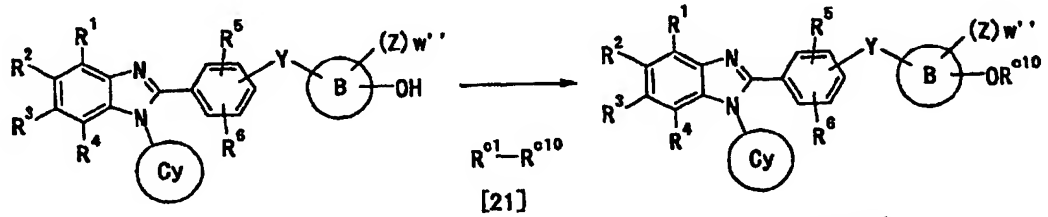
[II-2-5] [20] [II-2-6]

wherein ring Z"-M is aryl metal compound, ring Z" moiety is optionally substituted C_{6-14} aryl or optionally substituted heterocyclic group corresponding to substituent Z, and the metal moiety contains boron, zinc, tin, magnesium and the like, such as phenylboronic acid, w" is 0, 1 or 2, and other symbols are as defined above.

[0204] The compound [II-2-5] obtained in the same manner as in the above-mentioned Production Method is reacted with aryl metal compound [20] in a solvent such as DMF, acetonitrile, 1,2-dimethoxyethane, THF, toluene, water and the like in the presence of a palladium catalyst such as tetrakis(triphenylphosphine)-palladium, bis(triphenylphosphine) palladium(II) dichloride, palladium acetate - triphenylphosphine and the like, a nickel catalyst such as nickel chloride, [1,3-bis(diphenylphosphino)-propane]nickel(II) chloride and the like, and a base such as potassium carbonate, potassium hydrogencarbonate, sodium hydrogencarbonate, potassium phosphate, triethylamine and the like at room temperature or with heating, to give compound [II-2-6].

Production Method 4-2

[0205] Conversion of hydroxyl group to ether



[II-2-7] [21] [II-2-8]

wherein R^{c10} is $-R^{a20}$ or $-(CH_2)_p-COR^{a21}$ corresponding to substituent Z, and other symbols are as defined above.

[0206] The compound [II-2-7] obtained in the same manner as in the above-mentioned Production Method is reacted with compound [21] in the same manner as in Production Method 3-1 to give compound [II-2-8].

Production Method 4-3

[0207] Synthesis in advance of ring B part such as compound [13] in Production Method 3-1

Example 62

<Synthesis of 6-(benzenesulfonylcarbamoyl)-1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methylbenzimidazole (62)>

[0195] In the same manner as in Example 1, 217 mg of the title compound were formed as colorless crystals from 220 mg of 6-carboxy-1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methylbenzimidazole and 141 mg of benzenesulfonamide.
[Properties of Compound (62)]
^{1}H-NMR ($CDCl_3$, δ ppm): 2.57 (3H, s), 5.44 (2H, s), 6.39 (1H, d, J=8 Hz), 7.32 (1H, d, J=8 Hz), 7.52-7.57 (2H, m), 7.62-7.68 (2H, m), 7.73-7.78 (3H, m), 8.14 (2H, d, J=8 Hz).
MASS(ESI): m/z 506 (M-1).

Example 63

<Synthesis of 1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methyl-6-((3-methylbenzene)sulfonylcarbamoyl)benzimidazole (63)>

[0196] In the same manner as in Example 1, 223 mg of the title compound were formed as colorless crystals from 220 mg of 6-carboxy-1-(2-chloro-4-trifluoromethylbenzyl)-2-methylbenzimidazole and 358 mg of (3-methylbenzene) sulfonamide.
[Properties of Compound (63)]
^{1}H-NMR($CDCl_3$-MeOH, δ ppm): 2.43(3H, s), 2.56(3H, s), 5.47(2H, s), 6.43(1H, d, J=8 Hz), 7.35(1H, d, J=8 Hz), 7.40-7.43(2H, m), 7.72-7.82(4H, m), 7.88-7.94(2H, m).
MASS(ESI): m/z 520 (M-H).
mp: 275-277°C.

Example 64

<Synthesis of 1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methyl-6-((E)-(2-phenylethene)sulfonylcarbamoyl) benzimidazole (64)>

[0197] In the same manner as in Example 1, 226 mg of the title compound were formed as colorless crystals from 220 mg of 6-carboxy-1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methylbenzimidazole and 383 mg of (E)-(2-phenylethene)sulfonamide.
[Properties of Compound (64)]
^{1}H-NMR($CDCl_3$-MeOH, δ ppm): 2.58(3H, s), 5.49(2H, s), 6.45(1H, d, J=8 Hz), 7.17(1H, d, J=15 Hz), 7.36-7.44(4H, m), 7.52-7.55(2H, m), 7.71-7.85(5H, m).
MASS(ESI): m/z 532 (M-H).
mp: 285-286°C.

Example 65

<Synthesis of 1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methyl-6-((5-chloro-2-thiophene)sulfonylcarbamoyl) benzimidazole (65)>

[0198] In the same manner as in Example 1, 210 mg of the title compound were formed as colorless crystals from 220 mg of 6-carboxy-1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methylbenzimidazole and 413 mg of (5-chloro-2-thiophene)sulfonamide.
[Properties of Compound (65)]
^{1}H NMR($CDCl_3$-MeOH, δ ppm): 2.60(3H, s), 5.55(2H, s), 6.52(1H, d, J=8 Hz), 6.98(1H, d, J=3 Hz), 7.40(1H, d, J=8 Hz), 7.72-7.80(3H, m), 7.86(1H, d, J=8 Hz), 7.92(1H, s).
MASS(ESI): m/z 546 (M-1).
mp: >300°C.

Example 66

<Synthesis of 1-(2-chloro-4-(N-methyl-N-(1-pentyl)amino)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl) benzimidazole (66)>

[0199] In the same manner as in Example 1, 130 mg of the title compound were formed as colorless crystals from 170 mg of 6-carboxy-1-(2-chloro-4-(N-methyl-N-(1-pentyl)amino)benzyl)-2-methylbenzimidazole and 96 mg of 1-pentanesulfonamide.

[Properties of Compound (66)]

^{1}H-NMR ($CDCl_3$, δ ppm): 0.89 (3H, t, J=7 Hz), 0.89 (3H, t, J=7 Hz). 1.20-1.70 (10H, m), 1.80-1.94 (2H, m), 2.61 (3H, s), 2.89 (3H, s), 3.24 (2H, t, J=7 Hz), 3.51-3.62 (2H, m), 5.35 (2H, s), 6.30-6.42 (2H, m), 6.70 (1H, d, J=1 Hz), 7.67 (1H, dd, J=1, 8 Hz), 7.74 (1H, d, J=8 Hz), 7.84 (1H, d, J=1 Hz).

MASS(ESI): m/z 531 (M-1).

Example 67

<Synthesis of 1-(2-chloro-4-(N-methyl-N-(1-pentyl)amino)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl) benzimidazole (67)>

[0200] In the same manner as in Example 1, 22 mg of the title compound were formed as a colorless powder from 125 mg of 6-carboxy-1-(2-chloro-4-(N-methyl-N-(1-pentyl)amino)benzyl)-2-methylbenzimidazole and 80 mg of (4-methylbenzene)sulfonamide.

[Properties of Compound (67)]

^{1}H-NMR ($CDCl_3$, δ ppm): 0.89 (3H, t, J=7 Hz), 1.19-1.40 (4H, m), 1.45-1.60 (2H, m), 2.42 (3H, s), 2.56 (3H, s), 2.88 (3H, s), 3.23 (2H, t, J=7 Hz), 5.27 (2H, s), 6.25 (1H, d, J=8 Hz), 6.32 (1H, dd, J=1, 8 Hz), 6.66 (1H, d, J=1 Hz), 7.32 (2H, d, J=8 Hz), 7.57-7.69 (2H, m), 7.81 (1H, s), 8.01 (2H, d, J=8 Hz).

MASS(ESI): m/z 553 (M+1).

Example 68

<Synthesis of 1-(4-(N-1-butyrylamino)-2-chlorobenzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole (68)>

[0201] In the same manner as in Example 1, 158 mg of the title compound were formed as colorless crystals from 210 mg of 1-(4-(N-1-butyrylamino)-2-chlorobenzyl)-6-carboxy-2-methyl-benzimidazole and 123 mg of 1-pentanesulfonamide.

[Properties of Compound (68)]

^{1}H-NMR (DMSO-d_6, δ ppm): 0.81 (3H, t, J=7 Hz), 0.89 (3H, t, J=7 Hz), 1.18-1.44 (4H, m), 1.50-1.76 (4H, m), 2.26 (2H, t, J=7 Hz), 2.50 (3H, overlapped with DMSO-d_6), 3.50 (2H, t, J=7 Hz), 5.54 (2H, s), 6.50 (1H, d, J=8 Hz), 7.28 (1H, dd, J=1, 8 Hz), 7.67 (1H, d, J=8 Hz), 7.80 (1H, dd, J=1, 8 Hz), 8.00 (1H, d, J=1 Hz), 8.11 (1H, s).

MASS(ESI): m/z 517 (M-1).

Example 69

<Synthesis of 1-(4-(N-1-butyrylamino)-2-chlorobenzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl) benzimidazole (69)>

[0202] In the same manner as in Example 1, 102 mg of the title compound were formed as colorless crystals from 190 mg of 1-(4-(N-1-butyrylamino)-2-chlorobenzyl)-6-carboxy-2-methylbenzimidazole and 126 mg of (4-methylbenzene)sulfonamide.

[Properties of Compound (69)]

^{1}H-NMR ($CDCl_3$, δ ppm): 0.98 (3H, t, J=7 Hz), 1.74 (2H, tq, J=7, 7 Hz), 2.32 (2H, t, J=7 Hz), 2.41 (3H, s), 2.55 (3H, s), 5.32 (2H, s), 6.21 (1H, d, J=8 Hz), 7.00 (1H, dd, J=1, 8 Hz), 7.30 (2H, d, J=8 Hz), 7.55-7.66 (2H, m), 7.75 (1H, s), 7.85 (1H, d, J=1 Hz), 7.99 (2H, d, J=8 Hz).

MASS(ESI): m/z 537 (M-1).

Example 70

<Synthesis of 1-(2-chloro-4-morpholinobenzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole (70)>

[0203] 1-(4-bromo-2-chlorobenzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole (250 mg) was dissolved in 3 ml of toluene, to which 63 mg of sodium t-butyrate, 49 mg of morpholine, 2.2 mg of (R)-(+)-2,2'-bis (diphenylphosphino)-1,1'-binaphthyl, and 1.1 mg of tris(dibenzylideneacetone) dipalladium (0) were added in this order in a nitrogen atmosphere, and the solution was stirred at 100°C for 20 hours. The reaction solution was concentrated under reduced pressure, and water was added thereto. Hydrochloric acid (1 N) was added to the solution to adjust to a pH of 7, and the solution was extracted with a mixture of chloroform and methanol at a ratio of 4:1. The organic layer was washed with saturated brine, dried with anhydrous magnesium sulfate, and then concentrated under reduced pressure. The residue was subjected to silica-gel column chromatography and eluted with a mixture of chloroform and methanol at a ratio of 30:1. The desired fractions were concentrated under reduced pressure. The residue was dissolved in 3.0 ml of N,N-dimethylformamide, and 3.2 ml of water was gradually added thereto in an oil bath at 80°C. The solution was allowed to cool. The crystals precipitated were collected through filtration, and dried under reduced pressure while being heated to give 103 mg of the title compound as pale yellow crystals.
[Properties of Compound (70)]
^{1}H-NMR($CDCl_3$-MeOH, δ ppm): 2.42(3H, s), 2.56(3H, s), 3.12(4H, t, J=6 Hz), 3.83(4H, t, J=6 Hz), 5.33(2H, s), 6.28 (1H, d, J=8 Hz), 6.58(1H, dd, J=8, 2 Hz), 6.95(1H, d, J=2 Hz), 7.29-7.34(3H, m), 7.70(1H, s), 7.82(1H, s), 7.00(2H, d, J=8 Hz).
MASS(ESI): m/z 537 (M-H).
mp: 239-241°C.

Example 71

<Synthesis of 1-(2-chloro-4-morpholinobenzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole (71)>

[0204] In the same manner as in Example 70, 210 mg of the title compound were formed as pale yellow crystals from 373 mg of 1-(4-bromo-2-chlorobenzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole and 352 mg of morpholine.
[Properties of Compound (71)>
^{1}H-NMR($CDCl_3$, δ ppm): 0.88(3H, t, J=7 Hz), 1.26-1.47(4H, m), 1.80-1.90(2H, m), 2.59(3H, s), 3.13(4H, t, J=6 Hz), 3.56(2H, t, J=7 Hz), 3.82(4H, t, J=6 Hz), 3.36(2H, s), 6.35(1H, d, J=8 Hz), 6.60(1H, dd, J=8, 2 Hz), 6.94(1H, d, J=2 Hz), 7.67-7.73(2H, m), 7.84(1H, s).
MASS(ESI): m/z 517 (M-H).
mp: 205-207°C.

Example 72

<Synthesis of 1-(2-chloro-4-(methylthio)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole (72)>

[0205] In the same manner as in Example 1, 274 mg of the title compound were formed as colorless crystals from 260 mg of 6-carboxy-1-(2-chloro-4-(methylthio)benzyl)-2-methylbenzimidazole and 170 mg of 1-pentanesulfonamide.
[Properties of Compound (72)]
^{1}H-NMR ($CDCl_3$, δ ppm): 0.88 (3H, t, J=7 Hz), 1.28-1.48 (4H, in), 1.81-1.92 (2H, m), 2.46 (3H, s), 2.60 (3H, s), 3.55-3.60 (2H, m), 5.41 (2H, s), 6.29 (1H, d, J=8 Hz), 6.95 (1H, dd, J=1, 8 Hz), 7.32 (1H, d, J=1 Hz), 7.67 (1H, dd, J=1, 8 Hz), 7.76-7.81 (2H, m).
MASS(ESI): m/z 478 (M-1).

Example 73

<Synthesis of 1-(2-chloro-4-(methylthio)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole (73)>

[0206] In the same manner as in Example 1, 267 mg of the title compound were formed as colorless crystals from 250 mg of 6-carboxy-1-(2-chloro-4-(methylthio)benzyl)-2-methylbenzimidazole and 185 mg of (4-methylbenzene)sulfonamide.

[Properties of Compound (73)]
^{1}H-NMR (DMSO-d_6, δ ppm): 2.38 (3H, s), 2.46 (3H, s), 2.48 (3H, s), 5.54 (2H, s), 6.36 (1H, d, J=8 Hz), 7.11 (1H, dd, J=1, 8 Hz), 7.40-7.43 (3H, m), 7.63 (1H, d, J=8 Hz), 7.71 (1H, d, J=8 Hz), 7.87 (2H, d, J=8 Hz), 8.04 (1H, s).
MASS(ESI): m/z 498 (M-1).

Example 74

<Synthesis of 1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (74)>

[0207] In the same manner as in Example 1, 174 mg of the title compound were formed as a white powder from 204 mg of 6-carboxy-1-(2-chloro-4-(trifluoromethyl)benzyl)-2-methylbenzimidazole and 118 mg of N-1-propylsulfamide.
[Properties of Compound (74)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.79(3H, t, J=7 Hz), 1.43(2H, m), 2.50(3H, s), 2.84(2H, q, J=7 Hz), 5.69(2H, s), 6.59(1H, d, J=8 Hz), 7.63(1H, d, J=8 Hz), 7.69(1H, d, J=8 Hz), 7.69(1H, brs), 7.80(1H, d, J=8 Hz), 8.02(1H, s), 8.08(1H, s), 11.57(1H, brs).
Mass(ESI): m/e 487 (M-H).
mp: 202-203°C.

Example 75

<Synthesis of 1-(2-chloro-4-phenylbenzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (75)>

[0208] In the same manner as in Example 1, 0.238 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole and 0.122 g of N-1-propylsulfamide.
[Properties of Compound (75)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.4 Hz), 1.38-1.46(2H, m), 2.52(3H, s), 2.84(2H, d, J=6.7 Hz), 5.63(2H, s), 6.52(1H, d, J=8.2 Hz), 7.37(1H, t, J=7.3 Hz), 7.44(2H, t, J=7.3 Hz), 7.53(1H, dd, J=8.2 and 1.7 Hz), 7.62-7.68(4H, m), 7.80(1H, dd, J=8.5 and 1.5 Hz), 7.85(1H, d, J=1.6 Hz), 8.12(1H, s), 11.61(1H, brs).
IR(Nujol): 1661 cm^{-1}.
mp: 193.5-193.8°C.

Example 76

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole (76)>

[0209] In the same manner as in Example 1, 0.222 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole and 0.121 g of N-1-butylsulfamide.
[Properties of Compound (76)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.74(3H, t, J=7.3 Hz), 1.18-1.24(2H, m), 1.35-1.42(2H, m), 2.52(3H, s), 2.87(2H, q, J=6.6 Hz),.5.63(2H, s), 6.52(1H, d, J=8.2 Hz), 7.37(1H, t, J=7.1 Hz), 7.45(2H, t, J=7.7 Hz), 7.53(1H, d, J=8.1 Hz), 7.61-7.71 (4H, m), 7.79(1H, dd, J=8.6 and 1.4 Hz), 7.85(1H, d, J=1.7 Hz), 8.12(1H, s), 11.61(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 187.7-189.0°C.

Example 77

<Synthesis of 1-(2-chloro-4-phenylbenzyl)-6-((N-1-hexylaminosulfonyl)carbamoyl)-2-methylbenzimidazole (77)>

[0210] In the same manner as in Example 1, 0.159 g of the title compound were formed from 0.125 g of 6-carboxy-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole and 0.084 g of N-1-hexylsulfamide.
[Properties of Compound (77)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.74(3H, t, J=7.1 Hz), 1.09-1.22(6H, m), 1.37-1.43(2H, m), 2.53(3H, s), 2.87(2H, q, J=6.9 Hz), 5.63(2H, s), 6.51(1H, d, J=8.1 Hz), 7.38(1H, t, J=7.2 Hz), 7.45(2H, t, J=7.4 Hz), 7.53(1H, dd, J=8.1 and 1.6 Hz), 7.61-7.71(4H, m), 7.80(1H, dd, J=8.4 and 1.5 Hz), 7.85(1H, d, J=1.7 Hz), 8.12(1H, d, J=1.4 Hz), 11.58(1H, brs).
IR(Nujol): 1661 cm^{-1}.
mp: 178.2-180.0°C.

Example 78

<Synthesis of 6-((benzylaminosulfonyl)carbamoyl)-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole (78)>

[0211] In the same manner as in Example 1, 0.163 g of the title compound were formed from 0.130 g of 6-carboxy-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole and 0.098 g of N-benzylsulfamide.
[Properties of Compound (78)]
^{1}H-NMR(DMSO-d_6, δ ppm): 2.53(3H, s), 4.14(2H, d, J=5.9 Hz), 5.62(2H, s), 6.49(1H, d, J=8.1 Hz), 7.06(1H, t, J=7.2 Hz), 7.15(2H, t, J=7.4 Hz), 7.26(2H, d, J=7.3 Hz), 7.38(1H, t, J=7.2 Hz), 7.45(2H, t, J=7.3 Hz), 7.55(1H, d, J=8.2 Hz), 7.65(3H, m), 7.72(1H, d, J=8.6 Hz), 7.87(1H, d, J=1.6 Hz), 7.99(1H, s), 8.31(1H, brt), 11.58(1H, brs).
IR(Nujol): 1650 cm^{-1}.
mp: 178.8-180.3°C.

Example 79

<Synthesis of 1-(4-bromo-2-chlorobenzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole (79)>

[0212] In the same manner as in Example 1, 0.13 g of the title compound were formed from 0.20 g of 1-(4-bromo-2-chlorobenzyl)-6-carboxy-2-methylbenzimidazole and 0.08 g of N-ethylsulfamide.
[Properties of Compound (79)]
^{1}H-NMR(DMSO-d_6, δ ppm): 1.02(3H, t, J=7.2 Hz), 2.48(3H, s), 2.91-2.97(2H, m), 5.55(2H, s), 6.39(1H, d, J=8.4 Hz), 7.45(1H, dd, J=8.4 and 2.0 Hz), 7.65(1H, d, J=8.4 Hz), 7.66(1H, brs), 7.78(1H, dd, J=8.4 and 1.7 Hz), 7.85(1H, d, J=2.0 Hz), 8.06(1H, d, J=1.4 Hz), 11.57(1H, brs).
IR(Nujol): 1661 cm^{-1}.
mp: 200.7-201.3°C.

Example 80

<Synthesis of 1-(4-bromo-2-chlorobenzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (80)>

[0213] In the same manner as in Example 1, 0.12 g of the title compound were formed from 0.25 g of 1-(4-bromo-2-chlorobenzyl)-6-carboxy-2-methylbenzimidazole and 0.10 g of N-1-propylsulfamide.
[Properties of Compound (80)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.79(3H, t, J=7.4 Hz), 1.41-1.48(2H, m), 2.48(3H, s), 2.85(2H, q, J=6.9 Hz), 5.54(2H, s), 6.39(1H, d, J=8.4 Hz), 7.45(1H, dd, J=8.4 and 2.0 Hz), 7.65(1H, d, J=8.5 Hz), 7.68(1H, brs), 7.78(1H, dd, J=8.4 and 1.5 Hz), 7.85(1H, d, J=1.9 Hz), 8.06(1H, d, J=1.4 Hz), 11.57(1H, brs).
IR(Nujol): 1661 cm^{-1}.
mp: 198.1-198.7°C.

Example 81

<Synthesis of 1-(4-bromo-2-chlorobenzyl)-6-((N-1-butylaminosulfonyl)carbamoyl)-2-methylbenzimidazole (81)>

[0214] In the same manner as in Example 1, 0.151 g of the title compound were formed from 0.200 g of 1-(4-bromo-2-chlorobenzyl)-6-carboxy-2-methylbenzimidazole and 0.080 g of N-1-butylsulfamide.
[Properties of Compound (81)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.3 Hz), 1.20-1.28(2H, m), 1.37-1.44(2H, m), 2.87-2.92(2H, m), 5.54(2H, s), 6.38(1H, d, J=8.3 Hz), 7.44(1H, d, J=8.3 Hz), 7.66(1H, d, J=8.5 Hz), 7.69(1H, brs), 7.78(1H, d, J=8.5 Hz), 7.86(1H, s), 8.06(1H, s), 11.55(1H, brs).
IR(Nujol): 1661 cm^{-1}.
mp: 199.6-200.4°C.

Example 82

<Synthesis of 1-(4-bromo-2-chlorobenzyl)-2-methyl-6-((N-1-pentylaminosulfonyl)carbamoyl)benzimidazole (82)>

[0215] In the same manner as in Example 1, 0.16 g of the title compound were formed from 0.20 g of 1-(4-bromo-2-chlorobenzyl)-6-carboxy-2-methylbenzimidazole and 0.08 g of N-1-pentylsulfamide.

[Properties of Compound (82)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.76(3H, t, J=6.8 Hz), 1.17-1.22(4H, m), 1.38-1.44(2H, m), 2.49(3H, s), 2.87(2H, q, J=6.9 Hz), 5.54(2H, s), 6.38(1H, d, J=8.4 Hz), 7.44(1H, d, J=8.3 Hz), 7.62-7.71(2H, m), 7.78(1H, d, J=8.4 Hz), 7.85(1H, d, J=1.5 Hz), 8.06(1H, s), 11.55(1H, brs).
IR(Nujol): 1661 cm^{-1}.
mp: 194.9-196.0°C.

Example 83

<Synthesis of 6-((benzylaminosulfonyl)carbamoyl)-1-(4-bromo-2-chlorobenzyl)-2-methylbenzimidazole (83)>

[0216] In the same manner as in Example 1, 0.09 g of the title compound were formed from 0.200 g of 1-(4-bromo-2-chlorobenzyl)-6-carboxy-2-methylbenzimidazole and 0.098 g of N-benzylsulfamide.
[Properties of Compound (83)]
^{1}H-NMR(DMSO-d_6, δ ppm): 4.15(2H, d, J=6.0 Hz), 5.54(2H, s), 6.36(1H, d, J=8.4 Hz), 7.08(1H, t, J=7.2 Hz), 7.17(2H, t, J=7.6 Hz), 7.28(2H, d, J=7.8 Hz), 7.47(1H, d, J=8.2 Hz), 7.63(1H, d, J=8.4 Hz), 7.71(1H, d, J=8.5 Hz), 7.86(1H, s), 7.94(1H, s), 8.33(1H, brt), 11.57(1H, brs).
IR(Nujol): 1672 cm^{-1}.
mp: 191.1-191.8°C.

Example 84

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(methyloxy)benzyl)-2-methylbenzimidazole (84)>

[0217] In the same manner as in Example 1, 0.16 g of the title compound were formed from 0.18 g of 6-carboxy-1-(2-chloro-4-(methyloxy)benzyl)-2-methylbenzimidazole and 0.126 g of N-1-butylsulfamide.
[Properties of Compound (84)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.3 Hz), 1.23(2H, m), 1.40(2H, m), 1.40(2H, m), 2.49(3H, s), 2.88(2H, m), 3.73(3H, s), 5.50(2H, s), 6.50(1H, d, J=8.7 Hz), 6.82(1H, dd, J=8.7 and 2.5 Hz), 7.13(1H, d, J=2.5 Hz), 7.64(1H, d, J=8.5 Hz), 7.69(1H, t, J=5.7 Hz), 7.77(1H, dd, J=1.6 and 8.4 Hz), 8.07(1H, s), 11.57(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 185-188°C.

Example 85

<Synthesis of 1-(2-chloro-4-(ethyloxy)benzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole (85)>

[0218] In the same manner as in Example 1, 0.086 g of the title compound were formed from 0.150 g of 6-carboxy-1-(2-chloro-4-(ethyloxy)benzyl)-2-methylbenzimidazole and 0.070 g of N-ethylsulfamide.
[Properties of Compound (85)]
^{1}H-NMR(DMSO-d_6, δ ppm): 1.03(3H, t, J=7.3 Hz), 1.28(3H, t, J=6.9 Hz), 2.91-2.97(2H, m), 3.99(2H, q, J=7.0 Hz), 5.49(2H, s), 6.48(1H, d, J=8.6 Hz), 6.81(1H, dd, J=8.9 and 2.5 Hz), 7.11(1H, d, J=2.5 Hz), 7.64(1H, d, J=8.6 Hz), 7.66-7.70(1H, m), 7.77(1H, dd, J=8.6 and 1.5 Hz), 8.08(1H, s), 11.59(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 181.4-183.2°C.

Example 86

<Synthesis of 1-(2-chloro-4-(ethyloxy)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (86)>

[0219] In the same manner as in Example 1, 0.084 g of the title compound were formed from 0.150 g of 6-carboxy-1-(2-chloro-4-(ethyloxy)benzyl)-2-methylbenzimidazole and 0.065 g of N-1-propylsulfamide.
[Properties of Compound (86)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.79(3H, t, J=7.4 Hz), 1.27(3H, t, J=7.0 Hz), 1.43(2H, q, J=7.1 Hz), 2.82-2.87(2H, m), 3.99(2H, q, J=7.1 Hz), 5.49(2H, s), 6.48(1H, d, J=8.8 Hz), 6.81(1H, dd, J=8.8 and 2.4 Hz), 7.11(1H, d, J=2.5 Hz), 7.63(1H, d, J=8.5 Hz), 7.71(1H, brs), 7.77(1H, d, J=8.3 Hz), 8.06(1H, s), 11.56(1H, brs).
IR(Nujol): 1667 cm^{-1}.
MASS(FD): m/z 464 (M).

mp: 175.3-176.2°C.

Example 87

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(ethyloxy)benzyl)-2-methylbenzimidazole (87)>

[0220] In the same manner as in Example 1, 0.200 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-(ethyloxy)benzyl)-2-methylbenzimidazole and 0.115 g of N-1-butylsulfamide.
[Properties of Compound (87)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.4 Hz), 1.20-1.30(5H, m), 1.37-1.44(2H, m), 2.48(3H, s), 2.88(2H, q, J=6.8 Hz), 3.99(2H, q, J=7.0 Hz), 5.49(2H, s), 6.48(1H, d, J=8.7 Hz), 6.80(1H, dd, J=8.7 and 2.5 Hz), 7.11(1H, d, J=2.5 Hz), 7.66-7.70(2H, m), 7.77(1H, dd, J=8.4 and 1.6 Hz), 8.07(1H, d, J=1.4 Hz), 11.56(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 180.0-181.3°C.

Example 88

<Synthesis of 1-(2-chloro-4-(pentyloxy)benzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole (88)>

[0221] In the same manner as in Example 1, 0.188 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-(pentyloxy)benzyl)-2-methylbenzimidazole and 0.090 g of N-ethylsulfamide.
[Properties of Compound (88)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.86(3H, t, J=6.9 Hz), 1.02(3H, t, J=7.1 Hz), 1.27-1.37(4H, m), 1.62-1.70(2H, m), 2.90-2.97(2H, m), 3.93(2H, t, J=6.6 Hz), 5.49(2H, s), 6.48(1H, d, J=8.5 Hz), 6.81(1H, dd, J=8.6 and 2.0 Hz), 7.11(1H, d, J=2.5 Hz), 7.62-7.69(2H, m), 7.77(1H, d, J=8.6 Hz), 8.08(1H, s), 11.59(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 179.2-181.4°C.

Example 89

<Synthesis of 1-(2-chloro-4-(pentyloxy)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (89)>

[0222] In the same manner as in Example 1, 0.142 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-(pentyloxy)benzyl)-2-methylbenzimidazole and 0.100 g of N-1-propylsulfamide.
[Properties of Compound (89)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.79 (3H, t, J=7.4 Hz), 0.86(3H, t, J=6.8 Hz), 1.25-1.38(4H, m), 1.39-1.47(2H, m), 1.62-1.69(2H, m), 2.82-2.88(2H, m), 3.93(2H, t, J=6.5 Hz), 5.49(2H, s), 6.48(1H, d, J=8.7 Hz), 6.81(1H, dd, J=8.7 and 2.5 Hz), 7.11(1H, d, J=2.4 Hz), 7.64(1H, d, J=8.5 Hz), 7.68-7.72(1H, m), 7.77(1H, d, J=8.5 Hz), 8.07(1H, s), 11.57(1H, brs).
IR(Nujol): 1667 cm^{-1}.
MASS(FD): m/z 506 (M).
mp: 176.4-179.1°C.

Example 90

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(pentyloxy)benzyl)-2-methylbenzimidazole (90)>

[0223] In the same manner as in Example 1, 0.14 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-(pentyloxy)benzyl)-2-methylbenzimidazole and 0.10 g of N-1-butylsulfamide.
[Properties of Compound (90)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.4 Hz), 0.86(3H, t, J=7.2 Hz), 1.19-1.43(8H, m), 1.63-1.69(2H, m), 2.48(3H, s), 2.88(2H, q, J=6.8 Hz), 3.93(2H, t, J=6.5 Hz), 5.49(2H, s), 6.47(1H, d, J=8.6 Hz), 6.80(1H, dd, J=8.8 and 2.5 Hz), 7.11(1H, d, J=2.6 Hz), 7.62-7.69(2H, m), 7.77(1H, dd, J=8.4 and 1.6 Hz), 8.07(1H, s), 11.56(1H, brs).
IR(Nujol): 1672 cm^{-1}.
mp: 173.5-175.2°C.

Example 91

<Synthesis of 1-(2-chloro-4-(2-furyl)benzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole (91)>

[0224] In the same manner as in Example 1, 0.141 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole and 0.088 g of N-ethylsulfamide.
[Properties of Compound (91)]
^{1}H-NMR(DMSO-d_6, δ ppm): 1.01(3H, t, J=7.2 Hz), 2.89-2.95(2H, in), 5.59(2H, s), 6.56(1H, d, J=8.1 Hz), 6.59(1H, dd, J=3.4 and 1.9 Hz), 7.05(1H, d, J=3.4 Hz), 7.55(1H, dd, J=8.1 and 2.0 Hz), 7.64(1H, brs), 7.66(1H, d, J=8.4 Hz), 7.75 (1H, d, J=1.8 Hz), 7.79(1H, dd, J=8.4 and 1.5 Hz), 7.87(1H, d, J=1.6 Hz), 8.09(1H, d, J=1.4 Hz), 11.59(1H, brs).
IR(Nujol): 1667 cm^{-1}.
MASS(FD): m/z 472 (M).
mp: 190.5-192.2°C.

Example 92

<Synthesis of 1-(2-chloro-4-(2-furyl)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (92)>

[0225] In the same manner as in Example 1, 0.105 g of the title compound were formed from 0.200 g of 6-carboxy-1-(2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole and 0.098 g of N-1-propylsulfamide.
[Properties of Compound (92)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.4 Hz), 1.37-1.46(2H, m), 2.51(3H, s), 2.84(2H, q, J=6.4 Hz), 5.59(2H, s), 6.56(1H, d, J=8.2 Hz), 6.59(1H, dd, J=3.5 and 1.7 Hz), 7.05(1H, d, J=3.4 Hz), 7.54(1H, d, J=8.1 Hz), 7.66(1H, d, J=8.5 Hz), 7.68-7.71(1H, m), 7.76(1H, d, J=1.5 Hz), 7.78(1H, dd, J=8.3 and 1.5 Hz), 7.87(1H, d, J=1.5 Hz), 8.10(1H, s), 11.56 (1H, brs).
IR(Nujol) : 1656 cm^{-1}.
MASS(FD): m/z 486 (M).
mp: 177.8-180.2°C.

Example 93

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole (93)>

[0226] In the same manner as in Example 1, 0.23 g of the title compound were formed from 0.337 g of 6-carboxy-1-((2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole and 0.228 g of N-1-butylsulfamide.
[Properties of Compound (93)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.74(3H, t, J=7.3 Hz), 1.21(2H, m), 1.37(2H, m), 2.51(3H, s), 2.87(2H, m), 5.59(2H, s), 6.56(1H, d, J=8.1 Hz), 6.59(1H, m), 7.04(1H, d, J=3.3 Hz), 7.54(1H, d, J=8.2 Hz), 7.66(2H, m), 7.75(1H, s), 7.78(1H, d, J=8.4 Hz), 7.87(1H, s), 8.09(1H, s), 11.58(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 205.0-205.3°C.

Example 94

<Synthesis of 6-((benzylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole (94)>

[0227] In the same manner as in Example 1, 0.23 g of the title compound were formed from 0.337 g of 6-carboxy-1-((2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole and 0.279 g of N-benzylsulfamide.
[Properties of Compound (94)]
^{1}H-NMR(DMSO-d_6, δ ppm): 2.51(3H, s), 4.14(2H, d, J=5.7 Hz), 5.58(2H, s), 6.53(1H, d, J=8.2 Hz), 6.59(1H, m), 7.06 (2H, m), 7.15(2H, t, J=7.5 Hz), 7.27(2H, d, J=7.4 Hz), 7.57(1H, dd, J=8.1 and 1.4 Hz), 7.64 (1H, d, J=8.5 Hz), 7.72(1H, dd, J=8.6 and 1.4 Hz), 7.76(1H, d, J=1.1 Hz), 7.89(1H, d, J=1.5 Hz), 7.98(1H, s), 8.31(1H, m), 11.59(1H, brs).
IR(Nujol): 1656 cm^{-1}.
mp: 187.3-187.5° C.

Example 95

<Synthesis of 1-(2-chloro-4-ethylbenzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole (95)>

[0228] In the same manner as in Example 1, 0.045 g of the title compound were formed from 0.150 g of 6-carboxy-1-(2-chloro-4-ethylbenzyl)-2-methylbenzimidazole and 0.082 g of N-1-propylsulfamide.
[Properties of Compound (95)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.79(3H, t, J=7.4 Hz), 1.13(3H, t, J=7.3 Hz), 1.39-1.47(2H, m), 2.54-2.59(2H, m), 2.82-2.87 (2H, m), 5.54(2H, s), 6.39(1H, d, J=8.1 Hz), 7.06(1H, d, J=8.5 Hz), 7.40(1H, s), 7.65(1H, d, J=8.5 Hz), 7.67-7.71(1H, m), 7.78(1H, d, J=8.8 Hz), 8.07(1H, s), 11.55(1H, brs).
mp: 174.3-175.7°C.

Example 96

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-ethylbenzyl)-2-methylbenzimidazole (96)>

[0229] In the same manner as in Example 1, 0.076 g of the title compound were formed from 0.150 g of 6-carboxy-1-(2-chloro-4-ethylbenzyl)-2-methylbenzimidazole and 0.090 g of N-1-butylsulfamide.
[Properties of Compound (96)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.77(3H, t, J=7.3 Hz), 1.13(3H, t, J=7.4 Hz), 1.19-1.27(2H, m), 1.36-1.43(2H, m), 2.54-2.59 (2H, m), 2.88(2H, q, J=7.4 Hz), 5.53(2H, s), 6.38(1H, d, J=8.3 Hz), 7.06(1H, d, J=7.5 Hz), 7.40(1H, s), 7.63-7.68(2H, m), 7.77(1H, d, J=8.5 Hz), 8.06(1H, s), 11.55(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 169.3-171.0°C.

Example 97

<Synthesis of 6-((N-1-butylaminosulfonyl)carbamoyl)-1- (2-chloro-4-n-hexylbenzyl)-2-methylbenzimidazole (97)>

[0230] In the same manner as in Example 1, 0.092 g of the title compound were formed from 0.150 g of 6-carboxy-1-(2-chloro-4-hexylbenzyl)-2-methylbenzimidazole and 0.077 g of N-1-butylsulfamide.
[Properties of Compound (97)]
^{1}H-NMR(DMSO-d_6, δ ppm): 0.76(3H, t, J=7.4 Hz), 0.75-0.84(3H, m), 1.20-1.27(8H, m), 1.36-1.43(2H, m), 1.47-1.54 (2H, m), 2.50-2.55(2H, m), 2.86-2.90(2H, m), 5.53(2H, s), 6.38(1H, d, J=8.0 Hz), 7.04(1H, d, J=8.1 Hz), 7.38(1H, s), 7.64-7.71(2H, m), 7.78(1H, dd, J=8.4 and 2.0 Hz), 8.08(1H, s). 11.55(1H, brs).
IR(Nujol): 1667 cm^{-1}.
mp: 172.1-173.4°C.

Test Example

<Activity of decreasing blood sugar using db/db mice>

Test compounds

[0231] 1-(2-Chloro-4-(n-pentyloxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole - Compound(15)
[0232] 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole - Compound (76)

Animal used

[0233] Five-week-old female mice [C57BL/KsJ-dbm db+/db+, C57BL/KsJ-dbm +m/+m (Jackson Laboratory)] were purchased, and were kept for 2 to 3 weeks. Then, these mice were used in the test.

Preparation of an agent

[0234] A test compound was mixed with a powdered chow (CE-2, made by Nippon Clea) using a mortar. The mixing ratio was 0.01%. The mixed chow was changed twice a week for each group. The feed amount and the remaining

amount were recorded, and the intake was calculated from the difference therebetween.

Test schedule

[0235] The female db/db mice were grouped according to the body weight, the plasma glucose, and the plasma triglyceride concentrations. Then, the mixture containing the test compound was administered to the mice for 14 days (from 8 to 10 weeks old). In the morning on day 7 and day 14, blood was collected from the orbital venous plexus using heparinized glass capillary tubes (Chase Heparinized Capillary Tubes), and a plasma fraction was obtained through centrifugal separation. Plasma glucose, triglyceride, and insulin concentrations were measured on day 0 and day 14. Plasma glucose and triglyceride concentrations were measured on day 7. The body weight was measured on day 0, day 7, and day 14. After the final collection of the blood, the mice were killed using CO_2 gas.

Measurement method

[0236] The plasma glucose was measured by a glucose oxidase method (Glucose CII-Test Wako made by Wako Pure Chemical Industries, Ltd.) using from 10 to 15 μl of plasma. The plasma triglyceride concentration was measured by a GPO-p-chlorophenol method (Triglyceride G-Test Wako made by Wako Pure Chemical Industries, Ltd.) or a GPO-DAOS method (Triglyceride E-Test Wako) using from 10 to 15 μl of plasma. The above-mentioned measurements were conducted immediately after the blood collection. The plasma insulin concentration was measured by radioimmunoassay method (Phadesef Insulin RIA Kit made by Cabi Pharmacia) using 20 μl of plasma (which can be stored at -20°C).

Results

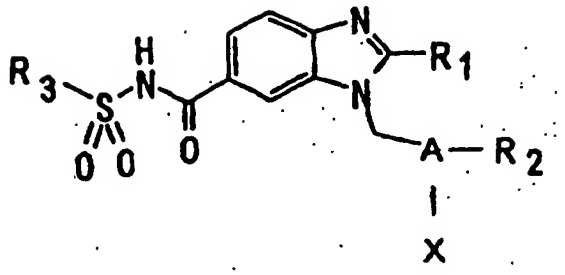
[0237] The difference in the plasma glucose and the plasma triglyceride concentrations betweeen the db/db mouse and the +/+ mouse was defined as 100%, and the rate (%) of decrease in the plasma glucose and the plasma triglyceride concentrations of the group to which the test compound was administered was calculated. The results were as follows: when 1 mg/kg of Compound (15) was administered, the rate of decrease in the plasma glucose was 79% and the rate of decrease in the plasma triglyceride was 69%; when 1 mg/kg of Compound (76) was administered, the rate of decrease in the plasma glucose was 71% and the rate of decrease in the plasma triglyceride was 98%.

INDUSTRIAL APPLICABILITY

[0238] Herein provided are novel benzimidazole derivatives and their pharmaceutically acceptable salts. These compounds and their salts, which are acceptable as medicine, have blood sugar level-depressing activity or PDE5-inhibiting activity, and are useful as therapeutic agents for impaired glucose tolerance, diabetes (type II diabetes), diabetic complications (e.g. diabetic gangrene, diabetic arthropathy, diabetic osteopenia, diabetic glomerulosclerosis, diabetic nephropathy, diabetic dermopathy, diabetic neuropathy, diabetic cataract, diabetic retinopathy, etc.) insulin-resistant syndrome (e.g., insulin receptor disorders, Rabson-Mendenhall syndrome, leprechaunism, Kobberling-Dunnigan syndrome, Seip syndrome, Lawrence syndrome, Cushing syndrome, acromegaly, etc.), polycystic ovary syndrome, hyperlipidemia, atherosclerosis, cardiovascular disorders (e.g., stenocardia, cardiac failure, etc.), hyperglycemia (e.g., abnormal saccharometabolism such as feeding disorders, etc.), pancreatitis, osteoporosis, hyperuricemia, hypertension, inflammatory bowel disease, skin disease accompanying abnormal differentation of epidermal cells, stenocardia, pulmonary hypertension, congestive heart failure, glomerulopathy (e.g., diabetic glomerulosclerosis, etc.), tubulointerstitial disorders (e.g., renopathy induced by FK506, cyclosporin, etc.), renal failure, atherosclerosis, angiostenosis (e.g., angiostenosis after percutaneous arterioplasty), distal angiopathy, cerebral apoplexy, chronic reversible obstructions (e.g., bronchitis, asthma (chronic asthma, allergic asthma), etc.), autoimmune disease, allergic rhinitis, urticaria, glaucoma, diseases characterized by enteromotility disorders (e.g., hypersensitive enteropathy syndrome, etc.), impotence (e.g., organic impotence, psychic impotence, etc.), nephritis, cachexia (e.g. progressive weight reduction due to lipolysis, myodegeneration, anaemia, edema, anorexia, and such in chronic diseases such as cancer, tuberculosis, endocrine diseases, and AIDS), pancreatitis, or post-PTCA restenosis. In addition, they, in combination with a retinoid, are effective for treating diseases associated with cell proliferative disorders including cancer, restenosis, and atherosclerosis.

Claims

1. A benzimidazole derivative of the following formula (I), or its salt:



(I)

wherein R_1 represents a lower alkyl group or a lower alkyloxy-lower alkyl group; R_2 represents a hydrogen atom, a halogen atom, an alkyl group having 1 to 8 carbon atoms, an aryl group, an aryl-lower alkyl group, an aryloxy-lower alkyl group, an alkyloxy group having 1 to 8 carbon atoms, a lower alkyloxy-lower alkyloxy group, a lower cycloalkyl-lower alkyloxy group, an aryl-lower alkyloxy group, an alkynyl group having 3 to 8 carbon atoms, a halo-lower alkyl group, a lower alkylthio group, a lower alkanoylamino group, an N-substituted lower alkylamino group, a thienyl group, a furyl group, or a morpholino group; R_3 represents a lower alkyl group, a lower alkenyl group, an aryl group, a lower alkylaryl group, an aryl-lower alkenyl group, a halothienyl group, a lower alkylamino group, or an aryl-lower alkylamino group;

A represents a benzene ring, a naphthalene ring, or a pyridine ring; and
X represents a halogen atom.

2. The benzimidazole derivative or its salt of claim 1, wherein A is a benzene ring.

3. The benzimidazole derivative or its salt of claim 2, wherein a lower alkyl or a lower alkenyl moiety of a lower alkyl group, a lower alkyloxy-lower alkyl group, an aryl-lower alkyl group, an aryloxy-lower alkyl group, a lower alkyloxy-lower alkyloxy group, a lower cycloalkyl-lower alkyloxy group, an aryl-lower alkyloxy group, a halo-lower alkyl group, a lower alkylthio group, an N-substituted lower alkylamino group, a lower alkanoylamino group, a lower alkenyl group, a lower alkylaryl group, an aryl-lower alkenyl group, a lower alkylamino group, and an aryl-lower alkylamino group has 1 to 6 carbon atoms; a lower cycloalkyl moiety of a lower cycloalkyl-lower alkyloxy group has 3 to 7 carbon atoms; and an aryl moiety of an aryl group, an aryl-lower alkyl group, an aryloxy-lower alkyl group, an aryl-lower alkyloxy group, and an aryl-lower alkylamino group is a phenyl group.

4. The benzimidazole derivative or its salt of claim 3, wherein R_1 is a methyl group or a methyloxymethyl group; R_2 is a hydrogen atom, an alkyl group having 2 to 7 carbon atoms, a phenyl group, a phenylethyl group, a phenyloxymethyl group, an alkyloxy group having 1 to 8 carbon atoms, a (2-methyloxyethyl)oxy group, a cyclopentylmethyloxy group, a benzyloxy group, an alkynyl group having 5 to 7 carbon atoms, a trifluoromethyl group, a methylthio group, a butyrylamino group, an N-methylpentylamino group, a thienyl group, a furyl group, or a morpholino group; and R_3 is a butyl group, a pentyl group, a pentenyl group, a phenyl group, a methylphenyl group, a phenylethenyl group, a chlorothienyl group, an amino group substituted with an alkyl group having 2 to 6 carbon atoms, or a benzylamino group.

5. The benzimidazole derivative or its salt of claim 1, wherein the benzimidazole derivative or its salt is selected from the group consisting of 1-(2,4-dichlorobenzyl)-2-methyl-6-((3-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-((1-bromonaphthalen-2-yl)methyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 6-(1-butanesulfonylcarbamoyl)-1-(4-bromo-2-chlorobenzyl)-2-methylbenzimidazole, 1-(4-bromo-2-chlorobenzyl)-2-methyl-6-((3-methylbenzene)sulfonylcarbamoyl)benzimidazole, 6-(1-butanesulfonylcarbamoyl)-1-(2-chloro-4-phenylbenzyl)-2-methylbenzimidazole, 1-(2-chloro-4-(2-phenylethyl)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(phenyloxymethyl)benzyl)-2-methyl-6-((E)-(1-pent-1-ene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(phenyloxymethyl)benzyl)-2-methyl-6-((E)-(2-phenylethene)sulfonylcarbamoyl)benzimidazole, 6-(1-butanesulfonylcarbamoyl)-1-(2-chloro-4-(phenyloxymethyl)benzyl)-2-methylbenzimidazole, 1-(2-chloro-4-(phenyloxymethyl)benzyl)-2-methyl-6-((3-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(n-octyloxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(n-octyloxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(n-hexyloxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(n-pentyloxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(n-pentyloxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(4-n-butyloxy-2-chlorobenzyl)-2-methyl-6-((4-methylbenzene)sulfonylcar-

bamoyl)benzimidazole, 1-(2-chloro-4-(n-propyloxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(n-propyloxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(methyloxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(methyloxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-((2-methyloxyethyl)oxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-((2-methyloxyethyl)oxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(cyclopentylmethyloxy)benzyl)-2-methyl-6-(1-pentanesulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(cyclopentylmethyloxy)benzyl)-2-methyl-6-((4-methylbenzene)sulfonylcarbamoyl)benzimidazole, 1-(2-chloro-4-(cyclopentylmethyloxy)benzyl)-2-methyl-6-((E)-1-pent-1-enesulfonylcarbamoyl)benzimidazole, 6-(benzenesulfonylcarbamoyl)-1-(4-benzyloxy-2-chlorobenzyl)-2-methylbenzimidazole, 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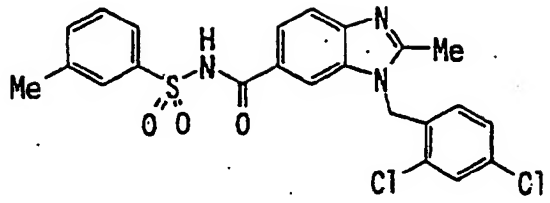
benzimidazole, 6-((benzylaminosulfonyl)carbamoyl)-1-(4-bromo-2-chlorobenzyl)-2-methylbenzimidazole, 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(methyloxy)benzyl)-2-methylbenzimidazole, 1-(2-chloro-4-(ethyloxy)benzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole, 1-(2-chloro-4-(ethyloxy)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole, 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(ethyloxy)benzyl)-2-methylbenzimidazole, 1-(2-chloro-4-(pentyloxy)benzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole, 1-(2-chloro-4-(pentyloxy)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole, 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(pentyloxy)benzyl)-2-methylbenzimidazole, 1-(2-chloro-4-(2-furyl)benzyl)-6-((N-ethylaminosulfonyl)carbamoyl)-2-methylbenzimidazole, 1-(2-chloro-4-(2-furyl)benzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole, 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole, 6-((benzylaminosulfonyl)carbamoyl)-1-(2-chloro-4-(2-furyl)benzyl)-2-methylbenzimidazole, 1-(2-chloro-4-ethylbenzyl)-2-methyl-6-((N-1-propylaminosulfonyl)carbamoyl)benzimidazole, 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-ethylbenzyl)-2-methylbenzimidazole, and 6-((N-1-butylaminosulfonyl)carbamoyl)-1-(2-chloro-4-n-hexylbenzyl)-2-methylbenzimidazole.

6. A pharmaceutical composition for preventing or treating impaired glucose tolerance, diabetes, diabetic complications, insulin-resistant syndrome, polycystic ovary syndrome, hyperlipidemia, atherosclerosis, cardiovascular disorders, hyperglycemia, pancreatitis, osteoporosis, hyperuricemia, hypertension, inflammatory bowel disease, skin disease accompanying abnormal differentation of epidermal cells, stenocardia, pulmonary hypertension, congestive heart failure, glomerulopathy, tubulointerstitial disorders, renal failure, atherosclerosis, angiostenosis, distal angiopathy, cerebral apoplexy, chronic reversible obstructions, autoimmune disease, allergic rhinitis, urticaria, glaucoma, diseases **characterized by** enteromotility disorders, impotence, nephritis, cachexia, pancreatitis, or post-PTCA restenosis, the pharmaceutical composition comprising, as an active ingredient, the benzimidazole derivative of any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof.

Figure 1.



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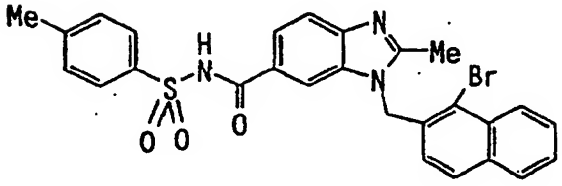

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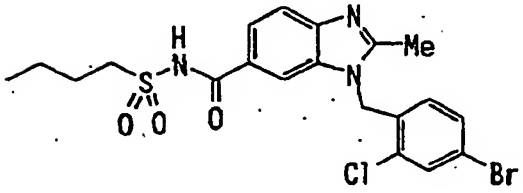

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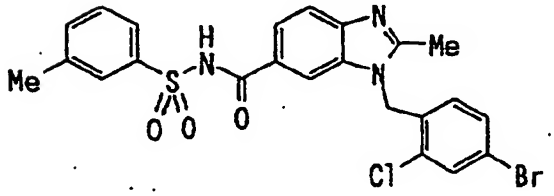

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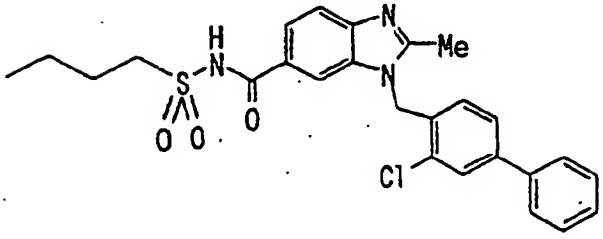

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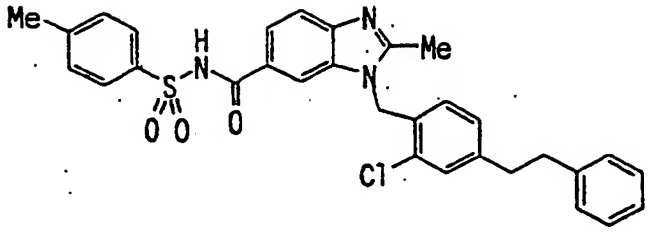
Figure 2



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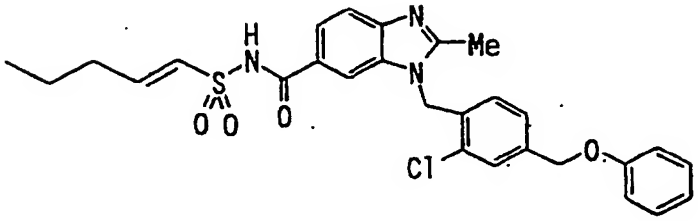

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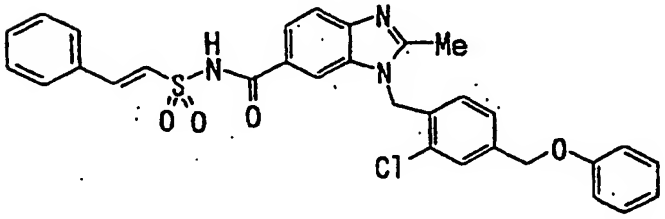

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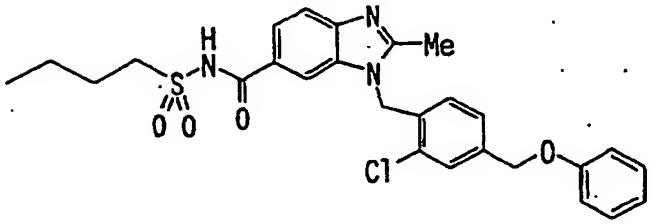

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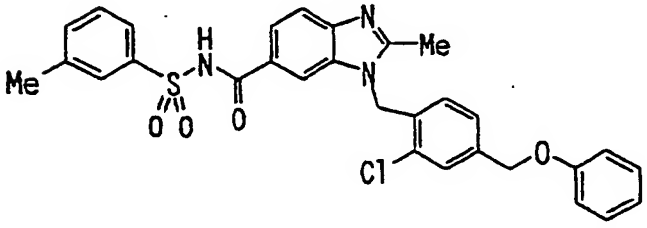

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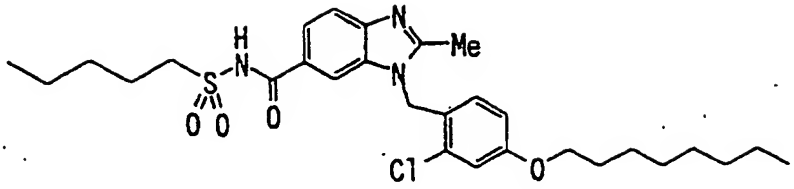

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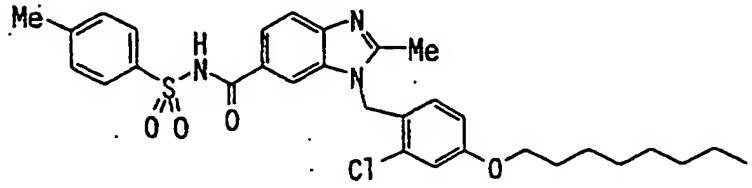

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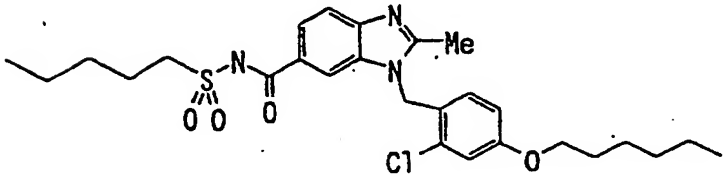

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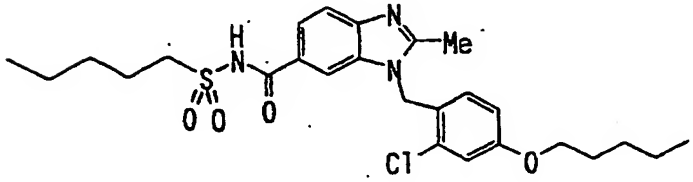

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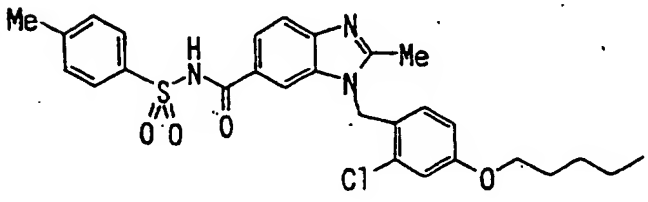

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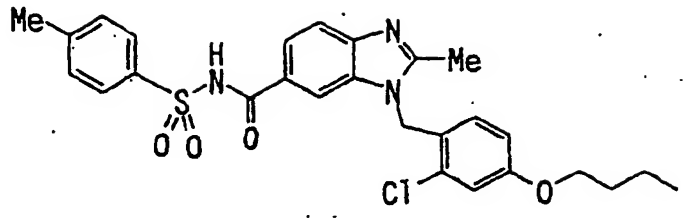

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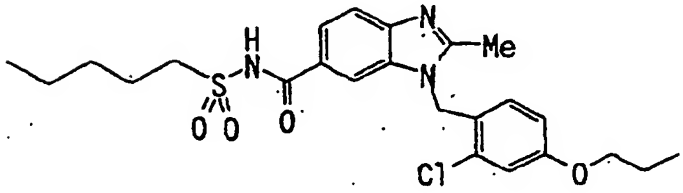

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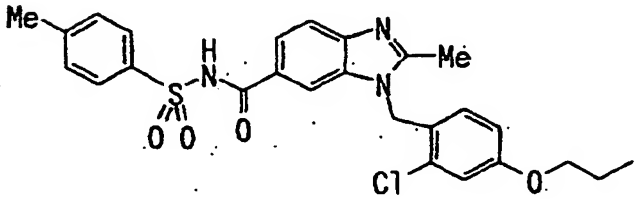

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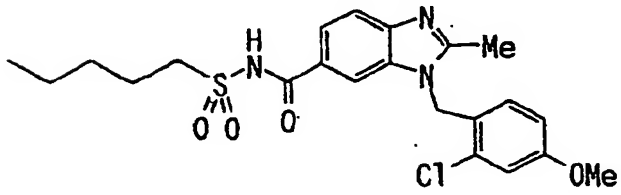

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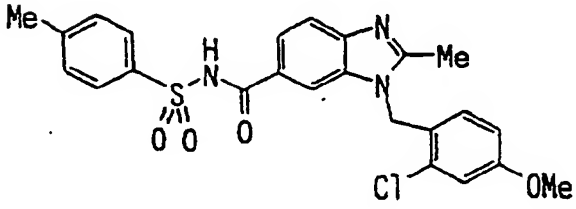

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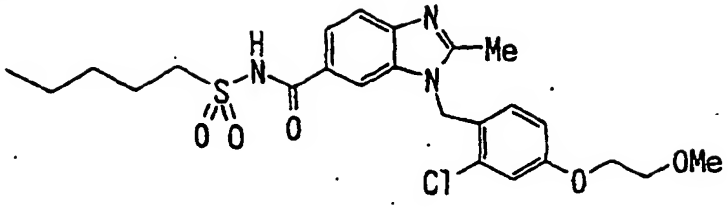

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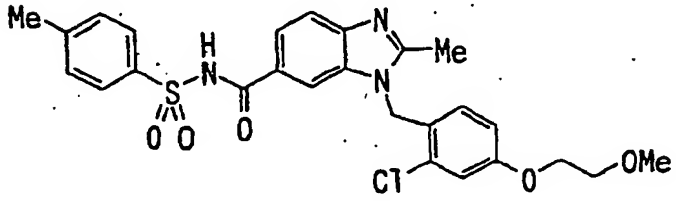

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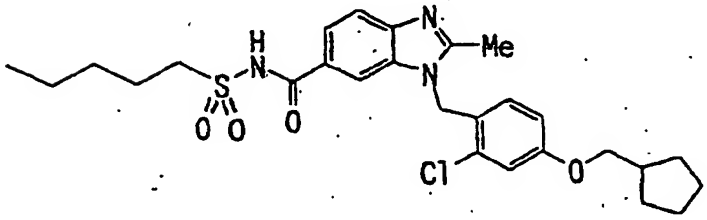

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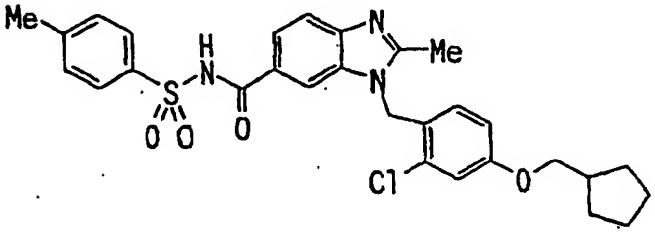

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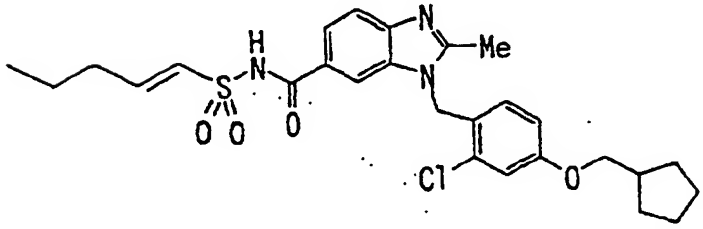

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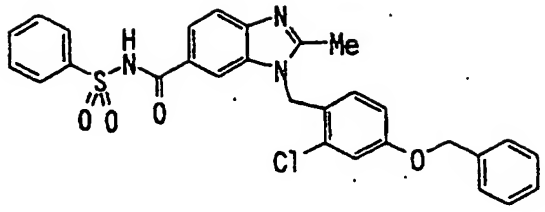

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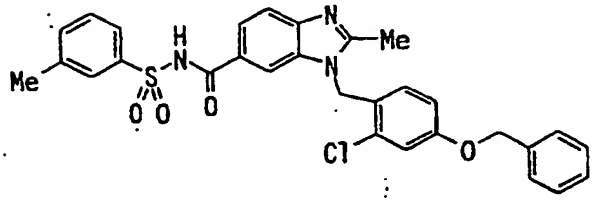

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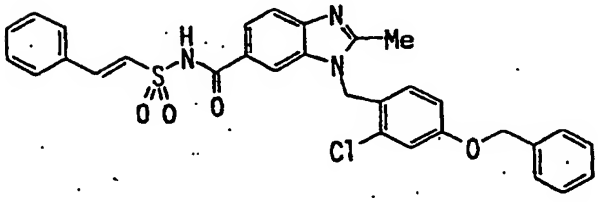

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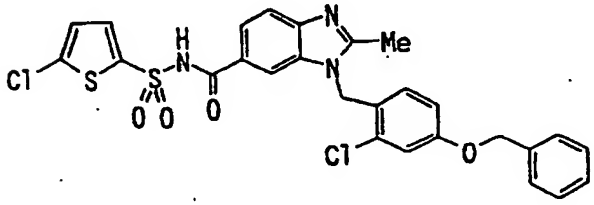

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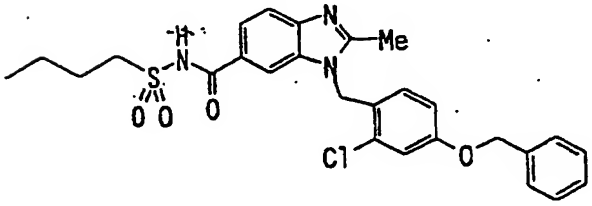

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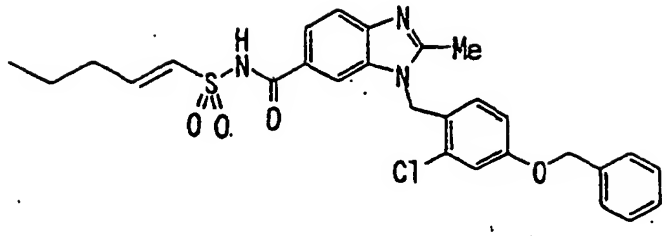

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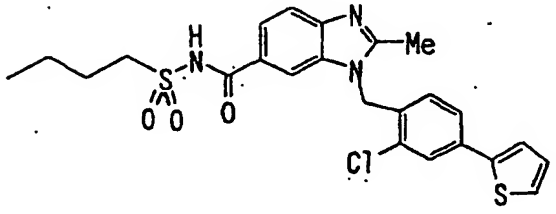

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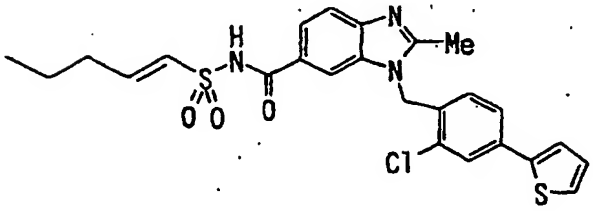

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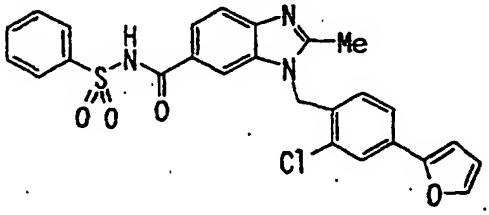

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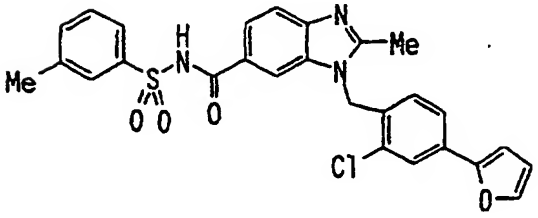

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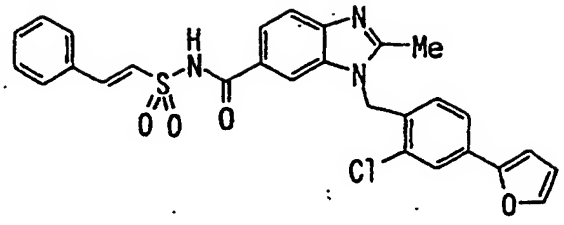

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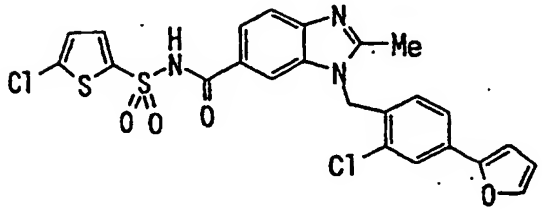

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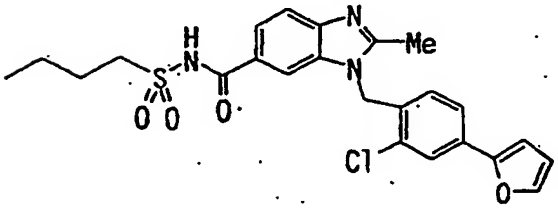

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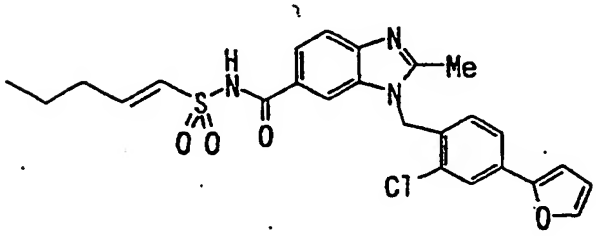

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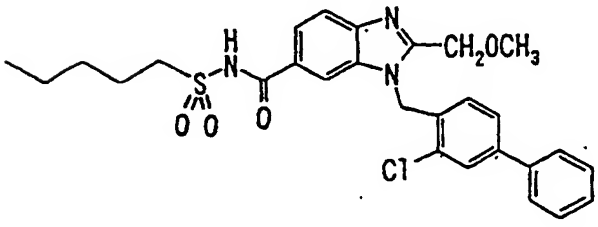

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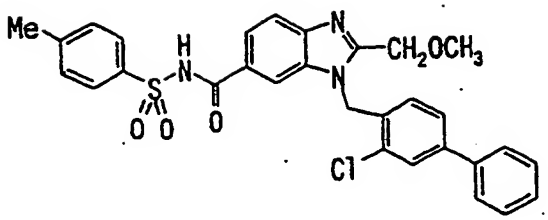

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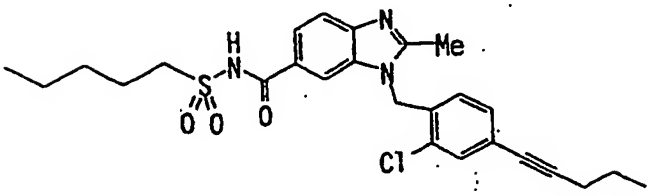

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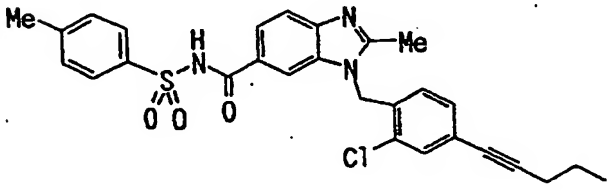

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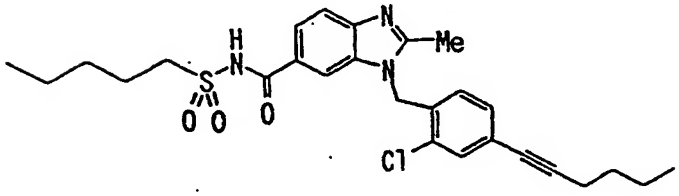

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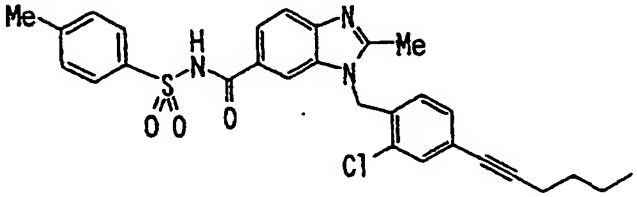

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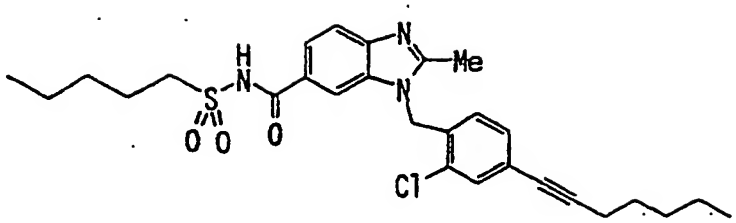

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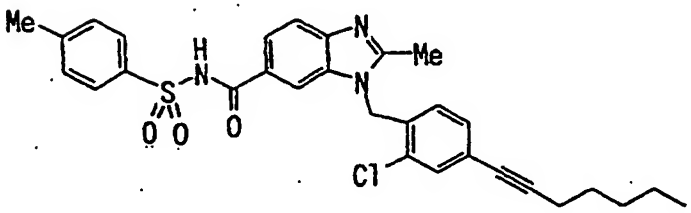

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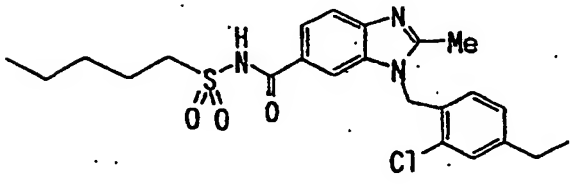

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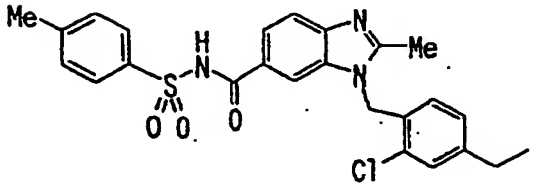

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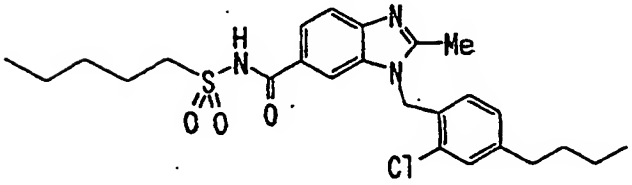

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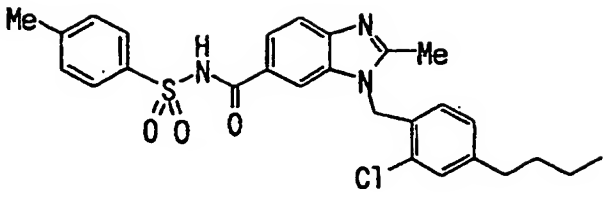

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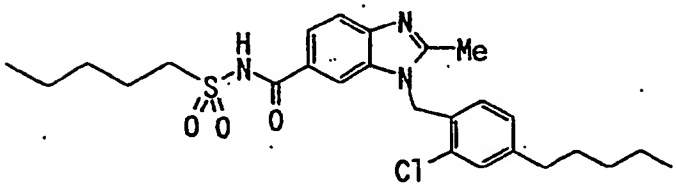

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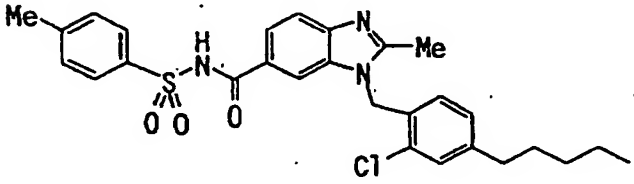

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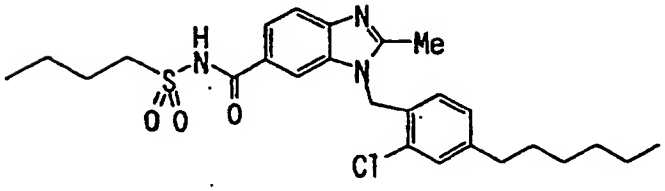

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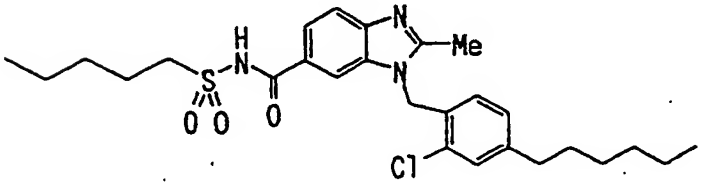

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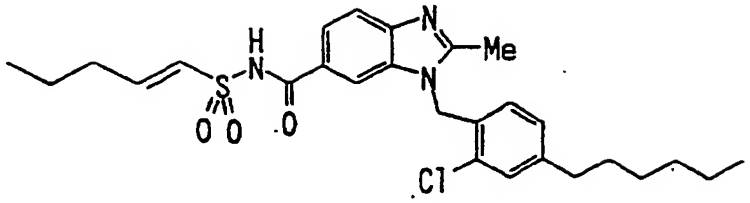

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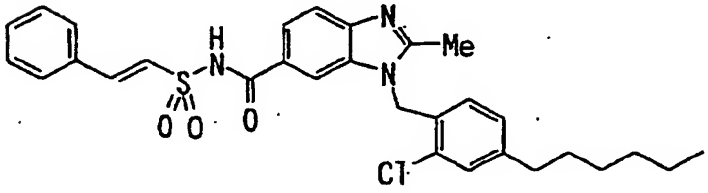

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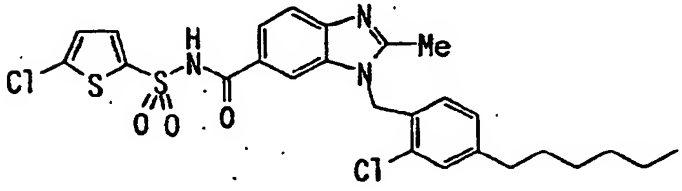

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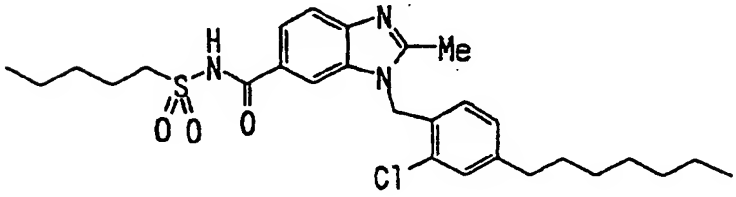

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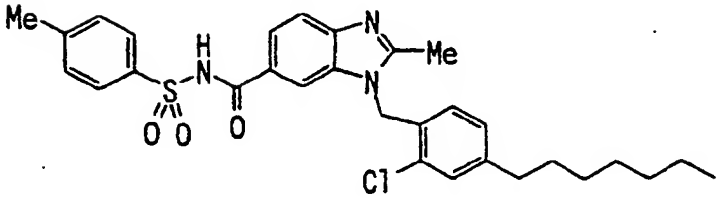

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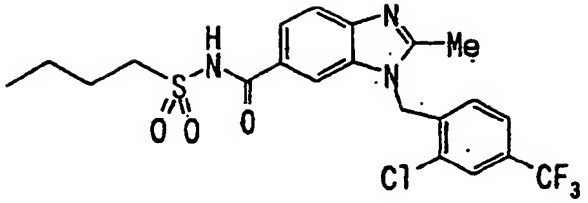

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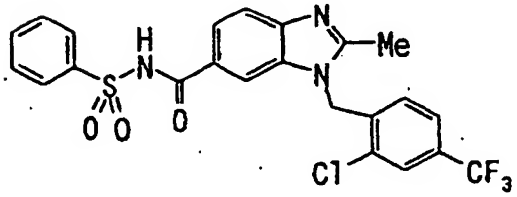

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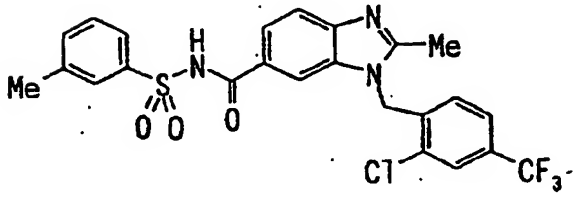

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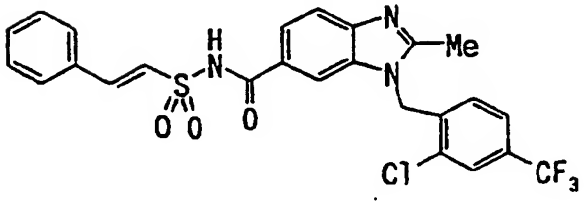

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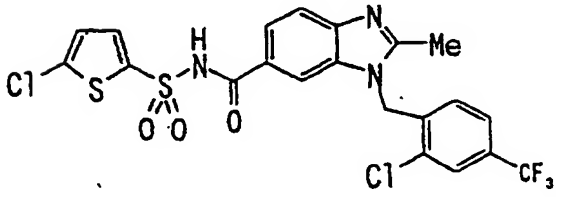

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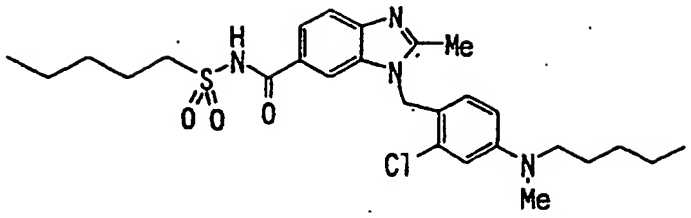
Figure 14



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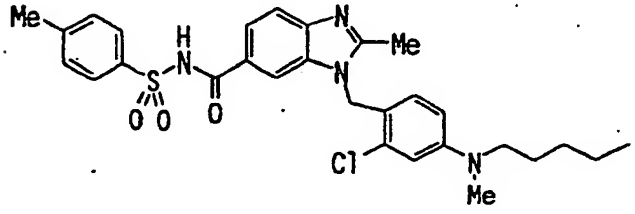

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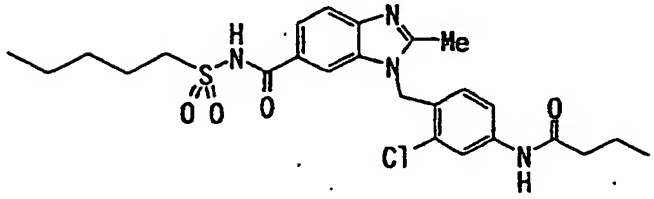

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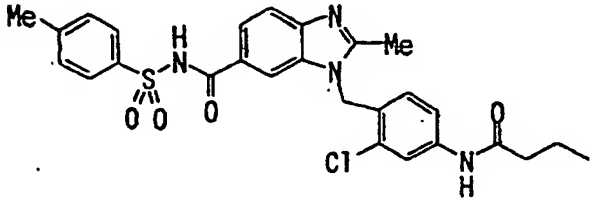

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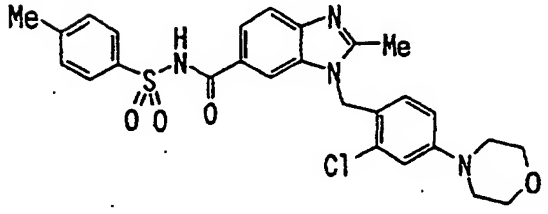

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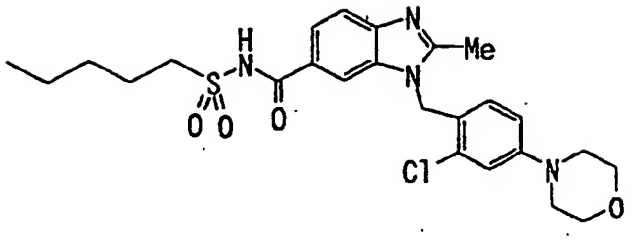

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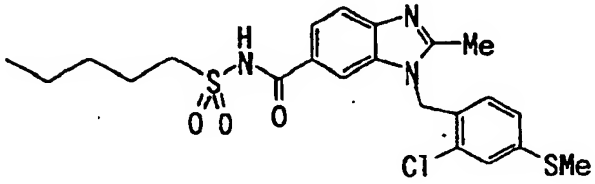

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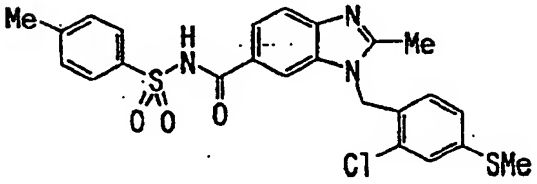

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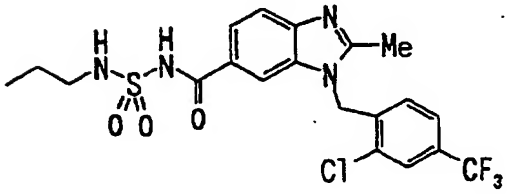

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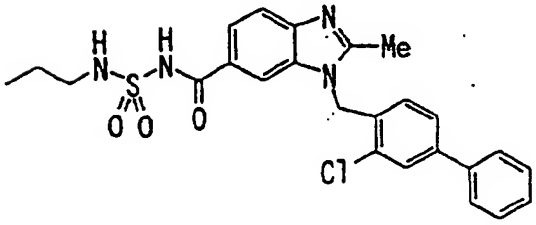

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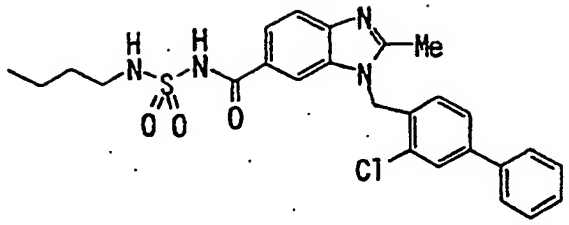
Figure 16



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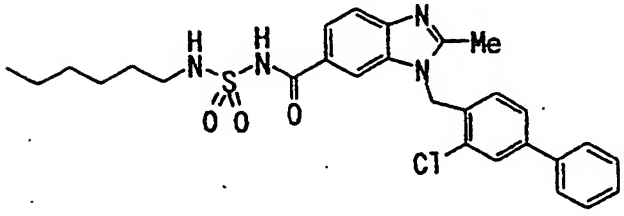

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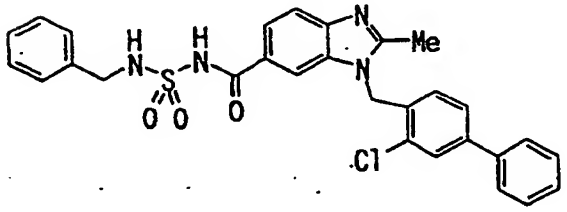

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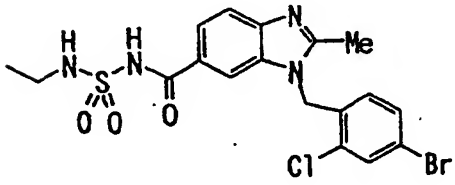

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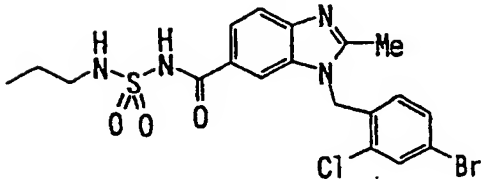

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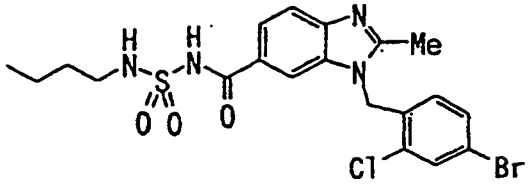

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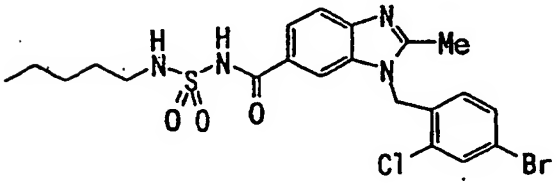

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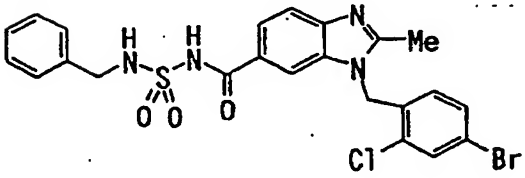

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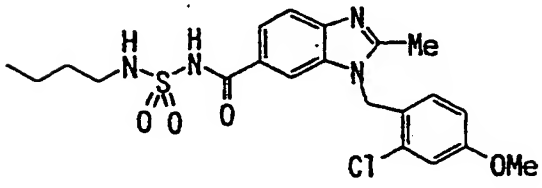

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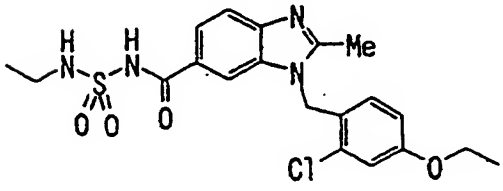

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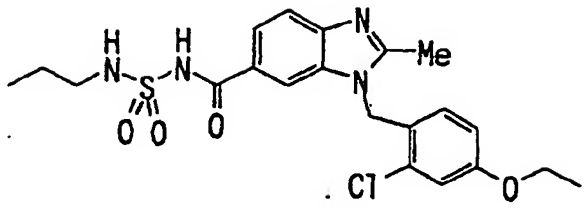
Figure 18



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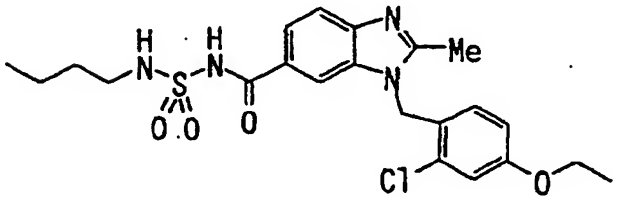

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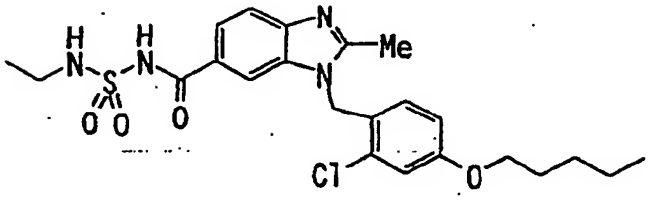

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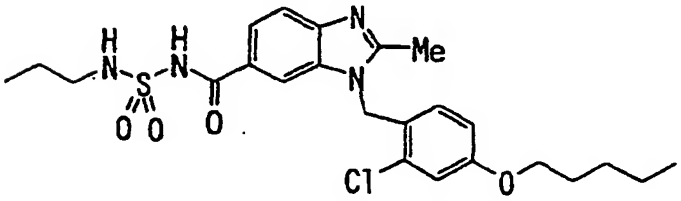

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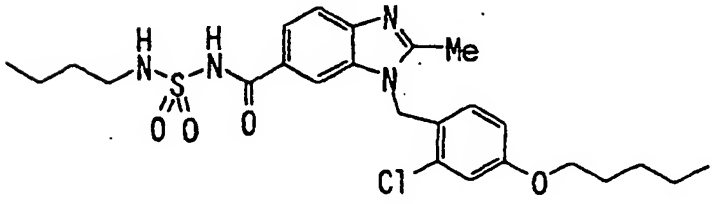

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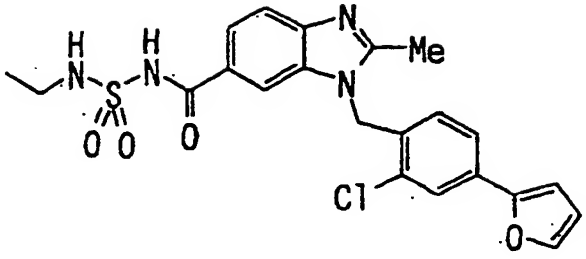
Figure 19



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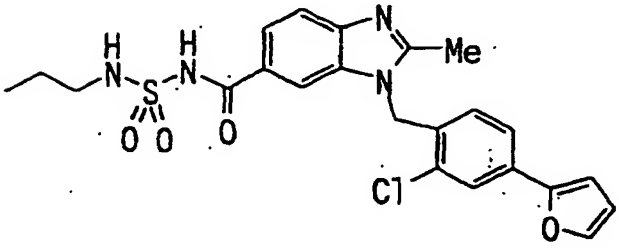

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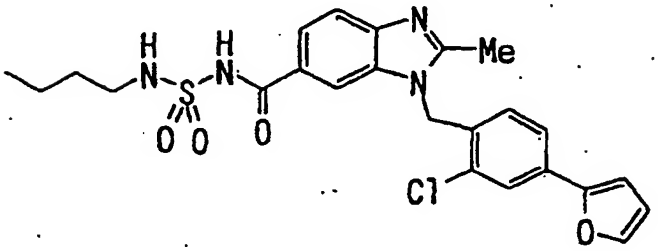

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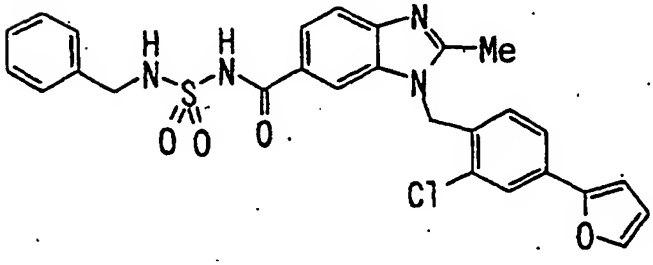

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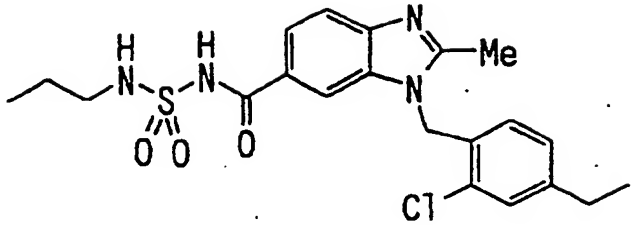
Figure 20



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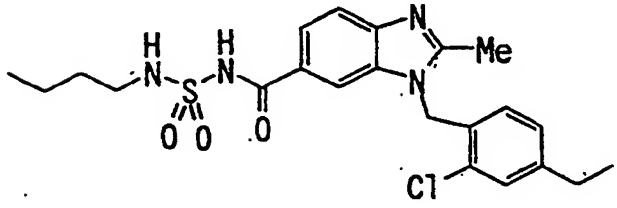

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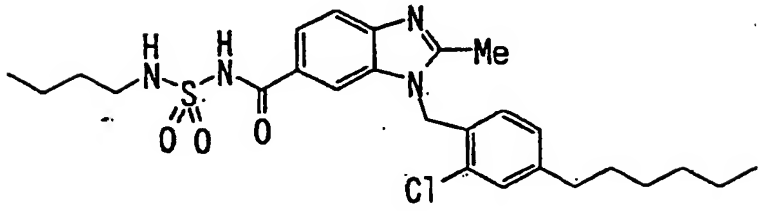

(97)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP99/07222

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] C07D235/08, C07D405/10, C07D409/10, C07D409/12, A61K31/4184, A61K31/5377, A61P3/06, A61P3/10, A61P9/10, A61P15/10, A61P27/06, A61P9/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] C07D235/08, C07D405/10, C07D409/10, C07D409/12, A61K31/4184, A61K31/5377, A61P3/06, A61P3/10, A61P9/10, A61P15/10, A61P27/06, A61P9/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAPLUS (STN)
REGISTRY (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO, 97/24334, A1 (Fujisawa Pharmaceutical Co., Ltd.), 10 July, 1997 (10.07.97), Claim 1 & CA, 2241186, A & EP, 882718, A	1-6
PX	WO, 99/00373, A1 (Fujisawa Pharmaceutical Co., Ltd.), 07 January, 1999 (07.01.99), Claim 1 & AU, 9879346, A	1-6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 March, 2000 (17.03.00)	04 April, 2000 (04.04.00)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)